Über dieses Buch

Dies ist ein digitales Exemplar eines Buches, das seit Generationen in den Regalen der Bibliotheken aufbewahrt wurde, bevor es von Google im Rahmen eines Projekts, mit dem die Bücher dieser Welt online verfügbar gemacht werden sollen, sorgfältig gescannt wurde.

Das Buch hat das Urheberrecht überdauert und kann nun öffentlich zugänglich gemacht werden. Ein öffentlich zugängliches Buch ist ein Buch, das niemals Urheberrechten unterlag oder bei dem die Schutzfrist des Urheberrechts abgelaufen ist. Ob ein Buch öffentlich zugänglich ist, kann von Land zu Land unterschiedlich sein. Öffentlich zugängliche Bücher sind unser Tor zur Vergangenheit und stellen ein geschichtliches, kulturelles und wissenschaftliches Vermögen dar, das häufig nur schwierig zu entdecken ist.

Gebrauchsspuren, Anmerkungen und andere Randbemerkungen, die im Originalband enthalten sind, finden sich auch in dieser Datei – eine Erinnerung an die lange Reise, die das Buch vom Verleger zu einer Bibliothek und weiter zu Ihnen hinter sich gebracht hat.

Nutzungsrichtlinien

Google ist stolz, mit Bibliotheken in partnerschaftlicher Zusammenarbeit öffentlich zugängliches Material zu digitalisieren und einer breiten Masse zugänglich zu machen. Öffentlich zugängliche Bücher gehören der Öffentlichkeit, und wir sind nur ihre Hüter. Nichtsdestotrotz ist diese Arbeit kostspielig. Um diese Ressource weiterhin zur Verfügung stellen zu können, haben wir Schritte unternommen, um den Missbrauch durch kommerzielle Parteien zu verhindern. Dazu gehören technische Einschränkungen für automatisierte Abfragen.

Wir bitten Sie um Einhaltung folgender Richtlinien:

+ *Nutzung der Dateien zu nichtkommerziellen Zwecken* Wir haben Google Buchsuche für Endanwender konzipiert und möchten, dass Sie diese Dateien nur für persönliche, nichtkommerzielle Zwecke verwenden.

+ *Keine automatisierten Abfragen* Senden Sie keine automatisierten Abfragen irgendwelcher Art an das Google-System. Wenn Sie Recherchen über maschinelle Übersetzung, optische Zeichenerkennung oder andere Bereiche durchführen, in denen der Zugang zu Text in großen Mengen nützlich ist, wenden Sie sich bitte an uns. Wir fördern die Nutzung des öffentlich zugänglichen Materials für diese Zwecke und können Ihnen unter Umständen helfen.

+ *Beibehaltung von Google-Markenelementen* Das "Wasserzeichen" von Google, das Sie in jeder Datei finden, ist wichtig zur Information über dieses Projekt und hilft den Anwendern weiteres Material über Google Buchsuche zu finden. Bitte entfernen Sie das Wasserzeichen nicht.

+ *Bewegen Sie sich innerhalb der Legalität* Unabhängig von Ihrem Verwendungszweck müssen Sie sich Ihrer Verantwortung bewusst sein, sicherzustellen, dass Ihre Nutzung legal ist. Gehen Sie nicht davon aus, dass ein Buch, das nach unserem Dafürhalten für Nutzer in den USA öffentlich zugänglich ist, auch für Nutzer in anderen Ländern öffentlich zugänglich ist. Ob ein Buch noch dem Urheberrecht unterliegt, ist von Land zu Land verschieden. Wir können keine Beratung leisten, ob eine bestimmte Nutzung eines bestimmten Buches gesetzlich zulässig ist. Gehen Sie nicht davon aus, dass das Erscheinen eines Buchs in Google Buchsuche bedeutet, dass es in jeder Form und überall auf der Welt verwendet werden kann. Eine Urheberrechtsverletzung kann schwerwiegende Folgen haben.

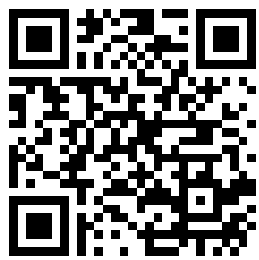
Über Google Buchsuche

Das Ziel von Google besteht darin, die weltweiten Informationen zu organisieren und allgemein nutzbar und zugänglich zu machen. Google Buchsuche hilft Lesern dabei, die Bücher dieser Welt zu entdecken, und unterstützt Autoren und Verleger dabei, neue Zielgruppen zu erreichen. Den gesamten Buchtext können Sie im Internet unter `http://books.google.com` durchsuchen.

This is a reproduction of a library book that was digitized by Google as part of an ongoing effort to preserve the information in books and make it universally accessible.

Google™ books

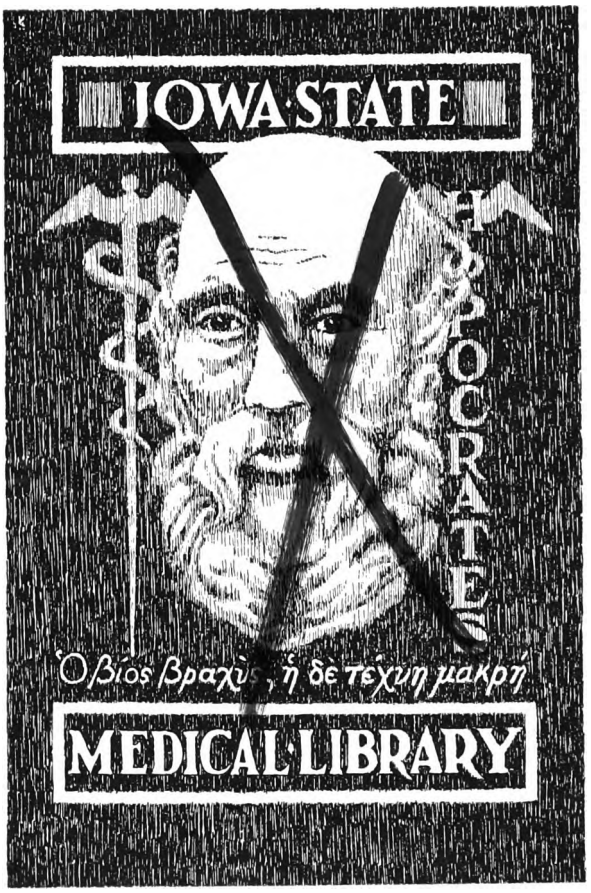
https://books.google.com



HEALTH SCIENCE

UNIVERSITY OF IOWA

LIBRARIES



Digitized by Google

UNIVERSITY OF IOWA
3 1858 019 780 752

DATE DUE

	AUG 1 1990 -9 00 AM		
	FEB 2 1 [illegible]		
	SEP 03 1993 -9 00 AM		

DEMCO 38-297

Digitized by Google

Digitized by Google

Digitized by Google

Digitized by Google

WITHDRAWN
MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

SEPTEMBER 4, 1948 PAGES 361 TO 400

THE LANCET

Offices: 7, ADAM STREET, ADELPHI, W.C.2

Telegrams: LANCET, RAND, LONDON **Telephone:** TEMPLE BAR 7228 and 7229

No. X OF VOL. II, 1948
No. 6523 VOL. CCLV

LONDON, SATURDAY, SEPTEMBER 4, 1948
Founded 1823 PUBLISHED WEEKLY Registered as a Newspaper

Pp. 80—Price 1s.
Annual Subscription:
Inland £2 2s. Abroad £2 10s.

Digitized by Google

PLATO FOLDER

RE-ORDER NO. 2-102½LK

28174

Digitized by Google

SEPT. 4, 1948 PAGES 361 TO 400

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6523 LONDON: SATURDAY, SEPTEMBER 4, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Accidental Intra-arterial Injection of Drugs — S. M. COHEN, F.R.C.S. (*to be concluded*) 361

Transorbital Leucotomy — WALTER FREEMAN, M.D. 371

Incontinence of Urine in the Aged — T. S. WILSON, M.D. 374

Spontaneous Rupture of the Rectum — C. P. ALLEN, F.R.C.S.E. 378

Congenital Torticollis in Identical Twins — A. E. STEVENS, F.R.C.S.E. 378

PRELIMINARY COMMUNICATION

Exsanguino-transfusion in Acute Leukæmia — A. PINEY, M.R.C.P. 379

SPECIAL ARTICLES

Intramedullary Nailing of Fractures — G. J. FRAENKEL, F.R.C.S. 387

International Congress on Population and World Resources 388

NEW INVENTIONS

A Matched Set of Needle-holders — HAROLD DODD, F.R.C.S. 380

REVIEWS OF BOOKS

Oral and Dental Diseases. Prof. H. H. Stones, F.D.S. R.C.S. 380

Vascular Diseases in Clinical Practice. Prof. I. S. Wright, M.D. 380

Pain. Prof. H. G. Wolff, M.D., Stewart Wolf, M.D. 380

Spasticity. Prof. H. W. Magoun, PH.D., Ruth Rhines PH.D. 380

Biology of Pathogenic Fungi. W. J. Nickerson, PH.D. 380

LEADING ARTICLES

FOOD AND PEOPLES 381

FUNCTION AND DYSFUNCTION OF THE BLADDER 382

MEDULLARY NAILING 383

ANNOTATIONS

Penicillin Ionisation Therapy 384

Inducement Fund 384

Histamine for Migraine 385

Infection by Train 385

Juvenile Osteochondritis of the Spine 386

Hospital Libraries 386

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 391

LETTERS TO THE EDITOR

Integration of Anatomy and Physiology (Prof. J. D. Boyd and others) 392

Latent Tetany Caused by BAL (Dr. D. K. O'Donovan) 393

Smaller and Better Practices (Dr. P. D. Mulkern; Dr. P. R. G. Howard) 393

Artificial Insemination (Dr. Robert Forbes) 394

Beds for Pulmonary Tuberculosis (Dr. L. E. Houghton; Dr. B. J. Douglas Smith, Dr. C. J. Stewart, Dr. W. E. Snell; Dr. Hermann Grunwald) 394

Medical Uses of Polythene (Dr. B. McNicholl; Mr. R. R. Foote, M.R.C.S.) 395

Professional Secrecy and Venereal Disease (Dr. Henry MacCormac) 396

Salaries in Government Service 396

The Alcoholic (Dr H. Pullar-Strecker) 396

M.R.C.P. Examination 396

Death while Bathing (Dr. F. Parkes Weber) 396

Appointments and Political Activities 397

Medical Records 397

OBITUARY

John Kay Jamieson 397

James Ernest Helme Roberts 398

Percy Roycroft Lowe 399

NOTES AND NEWS

Private Practice From Health Centres 399

Ophthalmic Prescriptions 399

Deeper and Deeper 399

Urine Testing without Heat 399

Medical Protection Society 399

J.A.M.A. 400

University of Leeds 400

University of Aberdeen 400

Royal College of Physicians of London 400

Edinburgh Post-Graduate Board for Medicine 400

Society of Apothecaries of London 400

Institute of Laryngology and Otology 400

Tuberculosis Course 400

Congress of Obstetrics and Gynæcology 400

Whitley Councils 400

North West Metropolitan Regional Tuberculosis Society 400

Supplies of Diphtheria Antitoxin 400

Medical Films 400

Appointments 400

Births, Marriages, and Deaths 400

MAJOR ENDOCRINE DISORDERS

by S. LEONARD SIMPSON, *M.A., M.D. (Cantab.), F.R.C.P. (London)*

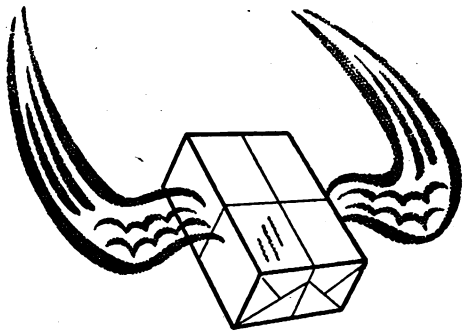
Physician, Willesden General Hospital, with charge of Diabetic and Endocrine Clinics; Endocrinologist, Princess Louise Children's Unit of St. Mary's Hospital; Consulting Physician and Endocrinologist, Soho and Samaritan Hospitals for Women

"A WORK WHICH CONTRIBUTES MUCH TO THE STUDY AND PRACTICE OF ENDOCRINOLOGY."—*Practitioner*

SECOND EDITION 574 pages 122 illustrations 42s. net

OXFORD UNIVERSITY PRESS

Digitized by Google



OXOID Therapeutical Preparations are despatched with unfailing promptness, and reach you with gratifying speed. This is a service you can rely on; every order is an emergency order.

Write, telephone or wire your instructions.

OXO LIMITED

MEDICAL DEPARTMENT

THAMES HOUSE, QUEEN ST. PLACE, LONDON, EC4

TELEPHONE CENTRAL 9761

IZAL
GERMICIDE

For more than half a century Newton Chambers, the makers of Izal Products, have devoted their skill and research to the safeguarding of public health

Newton, Chambers & Co. Ltd., Thorncliffe, Sheffield

FOR THE BUSY PRACTITIONER

The convenience of tablet medication is undoubtedly of marked value in the treatment of many conditions presented daily to the physician.

This is particularly true of alkaline therapy, where 'Milk of Magnesia' Tablets are a frequent and everyday prescription. In the busy dispensary, or for providing immediate symptomatic relief while visiting the patient's home, they present advantages readily appreciated by the practitioner.

Quickly dispensed, accurate in dosage and convenient to take during working hours, 'Milk of Magnesia' Tablets offer a simple yet efficacious means of combating gastric upset due to hyperchlorhydria.

SPECIAL PROFESSIONAL PACKS

For personal, surgery or dispensing use, a professional pack of 'Milk of Magnesia' Tablets is available. This contains 500 Tablets and costs 10/- (including tax) post free. Orders should be sent direct.

'MILK OF MAGNESIA' TABLETS

THE CHAS. H. PHILLIPS CHEMICAL CO., LTD., 1, WARPLE WAY, LONDON, W.3

★ *'Milk of Magnesia' is the trade mark of Phillips' preparation of magnesia.*

Digitized by Google

DES MOINES, IOWA 2017

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SOL. M. COHEN
M.A. Cape Town, F.R.C.S.
CONSULTANT SURGEON, GRAVESEND AND NORTH KENT HOSPITAL, GRAVESEND; FORMERLY SURGEON, SOUTHERN HOSPITAL, DARTFORD, KENT

IN 1943, while I was working on traumatic arterial spasm, my attention was drawn by Prof. R. R. Macintosh and Colonel Hedley Atkins to several tragedies following the accidental intra-arterial injection of soluble thiopentone ('Pentothal Sodium.') The cases were of interest not only from the point of view of the need for a rationale for the management of such limbs, but also because they suggested a means for producing traumatic arterial spasm experimentally.

A review of the cases has shown that, though spasm of a major vessel does not usually follow such injection, the development of extensive thrombosis (often late), distal arteriolar spasm, and severe œdema presented problems commonly met with in arterial injuries and disease. This paper is concerned chiefly with the detailed study of eight unpublished thiopentone cases and includes closer analysis of four of the published cases in which it has been possible to obtain pathological material, and further details of the findings at operation and the treatment. Collected cases of tragedies following intra-arterial injections of diagnostic and therapeutic media are also reviewed.

I wish to emphasise first of all, from a close study of the case-records and first-hand accounts from the anæsthetists, that these tragedies in no way reflect on the anæsthetists' competence and are not necessarily due to carelessness or bungling. This accident can happen to anyone. One anæsthetist has had the misfortune to be responsible for two such tragedies; and in one hospital, though the hazard was well recognised, there have been three tragedies and four other cases in which the injection was almost certainly intra-arterial but fortunately with no untoward results. The case-records indicate that there has been little groping for the vein, and the injection has often been particularly easy. Intra-arterial puncture is not followed, as is commonly imagined, by a gush of blood blowing off the syringe piston; those who have done arteriograms know that definite aspiration is often required. Nor is the crimson livery of arterial blood readily discerned in the yellowish solution. Moreover, the anæsthetist usually aspirates, momentarily only, a mere wisp of blood—and this under difficulties, for he is seldom permitted the luxury of a decent light while giving his injection.

Contrary to what is taught, puncture of the arterial wall is usually painless. I have done numerous arterial punctures for arteriography under local anæsthesia and, to test this point, have confined the anæsthetic solution to the skin only. The puncture alone is not felt; the intima appears to be insensitive. Large vessels may be painlessly tied. Puncture of a vessel is painful only in the case of arteries covered with a network of sensory nerves—e.g., the radial and common femoral. Lewis (1942) has shown, in animals, that barium chloride injected into the arterial lumen is painful only if allowed to reach the distal capillary tree. One finds the same thing in brachial arteriography: when 35% diodone is injected with the arterial circulation arrested by an inflated tourniquet, no pain is felt until 4–5 ml. has been injected; the patient then complains of a hot burning pain in the hand and fingers, and this continues as long as the tourniquet is kept inflated. Radiography shows that this small amount is adequate to fill the entire distal arterial tree. The pain is similar to, though not so well marked as, that following intra-arterial thiopentone; the quantity (4 ml.) represents the minimal amount of 10% thiopentone that has hitherto been reported to be followed by serious effects. It is a pointer to the anæsthetist to inject, as has been recommended (Macintosh and Heyworth 1943), say 2 ml., and pause a few moments for any complaint of pain.

It is strange that complications such as extensive thrombosis should follow injection into the swiftly moving arterial stream; for, if thiopentone was such an irritating corrosive, a far higher incidence of venous thrombosis would be expected, the venous tree, as every surgeon knows, thromboses all too readily on any damage. The explanation for this I do not yet know; but several factors may be responsible: the resistance of the arterial wall due to its relatively abundant muscle and elastic fibres; the temporary arrest of the arterial circulation by the inadequate release of the "venous" tourniquet; and the trapping of the solution in the arterial tree by vigorous flexion of the elbow after the injection.

SIGNIFICANCE OF VENOUS THROMBOSIS

Venous thrombosis, as Adams (1944) points out, is usually delayed; coming on from the fifth to the tenth day, and with a 5% solution there has been an incidence of 10 in 10,000 administrations; with the 2½% solution the complication is rare. In this country, Evans (1939) and Payne (1939) have reported isolated examples; Solomons (1945), using a 2½% solution, reported an incidence of 1 in 700 in acute battle casualties in a tropical area. The question has arisen whether extensive venous thrombosis may not alone lead to limb gangrene, for this is known to have followed the accidental injection of sclerosants into the deep veins of the leg (Erb 1944, Foote 1945, Luke and Miller 1948).

In several of the thiopentone cases the site of vessel puncture could not subsequently be found at operation, and there appears to have been no arterial leakage whatsoever. This is surprising, for anyone who has done arteriography will have observed that the vessel leaks considerably, the adjacent adventitia is usually heavily stained, and, even if the vessel is compressed rapidly after withdrawal of the needle, a hæmatoma bleb invariably forms in the adventitia. However, in some of the recorded tragedies following arteriography the puncture site has likewise not been visible (Leveuf 1938).

Deep venous thrombosis cannot be lightly dismissed as a possible factor responsible for death of the limb or other serious complication, such as Volkmann's contracture. Leriche (1945), Cohen (1946b), and Fontaine and Forster (1946) have commented that when the arterial circulation is poor, or in spasm, the onset of venous thrombosis will seal the fate of the limb; the increased venous pressure raises the intracapillary pressure, bringing the local circulation to a standstill. Venous obstruction alone, it is now believed, may lead to death of muscle from Volkmann's ischæmia; microscopically, the picture differs somewhat from that of the arterial lesion (Griffiths 1940), but the end-result—extensive fibrous-tissue infiltration—is the same (Bowden and Gutmann 1945, Albert and Mitchell 1943). Such deep thrombosis following prolonged blood-transfusion for severe hæmatemesis has been followed by Volkmann's contracture in the transfusing arm (F. R. Kilpatrick, personal communication). After the injection of thiopentone the venous thrombosis may be extensive and involve the deep veins as well by retrograde flow. With intravenous injection at the elbow phlebography shows clearly (fig. 1) that the solution does not merely continue its flow in equable fashion in the punctured vein but also owing to the situation of the vein valves, descends a considerable distance into the forearm and then spills over into the main interlacing venous net. Hewspear (1945) has described in detail a case where extensive

Digitized by Google

deep venous thrombosis followed the injection of thiopentone, and attributed this as in part due to the placing of the elbow in acute flexion (the hand being tucked behind the head) after the injection. I have seen an injection of thiopentone followed by an enormous œdematous forearm which took over nine months to subside. Such cases are rarely reported.

Anæsthetists need to be aware of the dangers of venous thrombosis; for, should intra-arterial injection be suspected, it would be unwise to risk thrombosing the veins in that arm, and any further thiopentone should be injected into the opposite arm. The present practice, too, of violently flexing the elbow after intravenous puncture can have no physiological sanction; local pressure and elevation of the limb are obviously what is needed. Moreover, such acute flexion of the elbow will obliterate the forearm pulses in most normal persons and may be responsible for the trapping and long-sustained action of any intra-arterial thiopentone.

INCIDENCE OF INTRA-ARTERIAL INJECTION OF THIOPENTONE

Intra-arterial injection, fortunately, has been a rare accident; within the last five years, after making full inquiries from leading anæsthetists and surgeons in this country, I have been able to gather only eight unreported cases. Lundy (1942) reports 3 intra-arterial punctures in 25,000 cases. In the B.L.A. campaign there was only one case (Porritt et al. 1945), and I am indebted to Brigadier A. E. Porritt, C.B.E., for the following report from Lieut.-Colonel J. H. Rink (anæsthetics adviser, 21 Army Group):

> "I only came across one case of intra-arterial injection of pentothal during the existence of 21 Army Group. The injection was undoubtedly made in the artery, and 3 ml. was given before it was realised; the anæsthesia was then continued with gas and oxygen. The patient complained of the typical intense pain along the course of the radial artery and in his hand, but he subsequently suffered no ill effects. I saw him next day, when he was normal in all respects, though no palliative injection of procaine was made, as some times recommended."

In the B.L.A. campaign, out of 181,000 casualties 55,000 required some form of front-line surgery; it may reasonably be presumed that most of these had thiopentone. One in 55,000 is probably a fair figure of the incidence of such major thiopentone tragedies in this country.

Particularly tragic is the fact that the thiopentone accidents have happened in the course of some relatively minor operation—e.g., for tonsils, ischiorectal abscess, hammer toe, uterine dilatation and curettage, knee cartilage, and, in one particularly pathetic case, colostomy; the helpless pitiful state of the latter patient with one arm can well be imagined. The 10% solution has been responsible usually for the serious effects, but in several of the tragedies the 5% solution was used. Several anæsthetists declare that they believe that they have accidentally injected the 5% solution into an artery without untoward effects; a well-marked limb flush has been the only subsequent complication. I have been unable to trace any case that has followed the use of hexobarbitone ('Evipan').

HEIGHT OF ASCENT OF RETROGRADE ARTERIAL INJECTION

A 35% solution of diodone was injected in retrograde fashion into the flowing arterial stream during an operation on the ulnar artery for arteriovenous aneurysm. The fluid was injected with full force through a two-way tap by an assistant after I had punctured the artery. Fig. 2 shows to what an enormous extent the artery was forcibly distended, and that the injected solution ascended into the brachial tree and was then redistributed. The exposure lasted $2^1/_2$ sec., the distal tree did not fill, and the solution was held. This explains why a retrograde arterial injection of thiopentone may have a somewhat long-continued action. Despite this violent stretching of the artery spasm of the major vessel was not maintained; when, with the needle kept in place, the injection was repeated in the time that it takes to change a plate, the major vessel was now of normal size and the distal arterial tree was already filling. This injection also lasted $2^1/_2$ sec. but was slow and gentle. Slow injection may explain why some of the intra-arterial thiopentone injections were not followed by serious lesions; the ready distal escape of the solution spared the major vessel and allowed the thiopentone to become diluted.

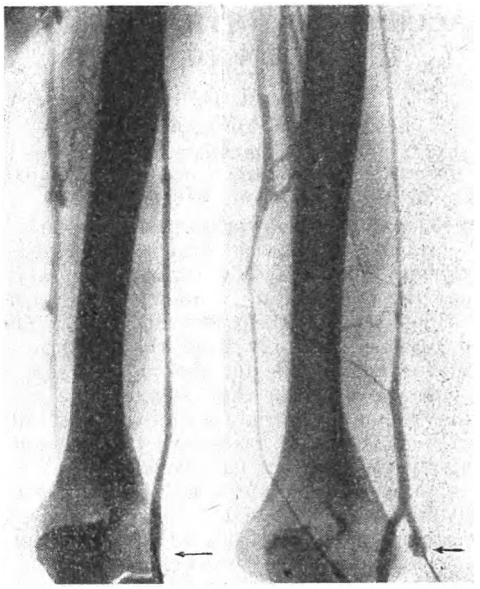


Fig. 1—Phlebograms: injection at elbow; arrows indicate needle points; note retrograde flow into forearm and spill over into connecting veins.

Arteriography also demonstrated that despite full-force injection the solution ascended against the flowing arterial stream not much more than 6–7 cm.; with gentler injection 3–4 cm. only (fig. 2). In the thiopentone cases operation has shown that the vessel may be filled with thrombus extending as high as 5 in. (12·5 cm.) above the elbow, and in one case up to the axilla. It is common experience that, with any trauma, arterial thrombosis does not ascend higher than the nearest proximal major collateral branch. This suggested that the high ascent of the thiopentone could only have been possible if the arterial circulation had been either completely or partially occluded during the injection. There were two possible causes for this: (1) inadequate release of the "venous" tourniquet; and (2) mechanical obliteration by the patient of the subclavian or axillary arteries by the clavicle or other local mechanism, owing to the position of the limb on the operating-table.

To investigate this, apparatus was designed to mimic fluid flowing at arterial pressure (fig. 3) conforming with the blood-flow in the brachial artery under resting conditions. Fluid was arranged to flow at 30–40 ml. per min., with air-pressure above the fluid at normal blood-pressure level. This flow was decided on in view of the plethysmograph studies of Barcroft and Edholm (1946) and Goetz (1946), who have shown that the blood-flow in the forearm under resting conditions is 3–4 ml. per min. per 100 c.cm. of forearm tissue. Since the average forearm volume is about 1000 c.cm., this means a flow of 30–40 ml. per min. through the brachial artery. This figure might well be doubled when the distal parts are warmed (J. McMichael, personal communication). A coloured solution was then injected with a 10 ml. syringe into the flowing stream. A similar injection was also tried when the air-pressure head above the fluid

Digitized by Google

was reduced to diastolic pressure. The coloured fluid did not rise more than 3–4 cm.; but, if the flow was cut off, the coloured fluid could be made to ascend 12 cm.

This observation confirmed my impression that, to inject the thiopentone high into the arm, there had been partial or complete obliteration of the pulse during the injection—due to arm or neck posture, or to the fact that the "venous" tourniquet, rubber, or assistant's compression had been inadequately released. A very transient arterial spasm which may give the solution an opportunity to ascend and be held can also follow too enthusiastic compression of the arm by the assistant. That this may have happened is shown by the report on one of the cases, that blistering subsequently developed at the site where the nurse had maintained pressure on the arm.

COMPRESSION OF SUBCLAVIAN AND AXILLARY ARTERIES

It is important for the anæsthetist to be aware of the mechanical factors which may temporarily obliterate or reduce the brachial and distal pulses. In a high percentage of normal persons bracing of the shoulders will lead to compression of the subclavian artery by the clavicle against the first rib and loss of distal pulse; a sandbag between the shoulders may do it. Strong downward traction of the elbow, such as firm tucking in of the hands under the buttocks, may obliterate the pulse, and gangrene of the hand is known to have followed this. A forceful deep inspiration will in some persons lead to the transient disappearance of the pulse; the mechanism is not clearly understood, but arrest of the pulse may be due to ascent of the first rib compressing the rib against the clavicle, or to the scissors-like gripping of the subclavian artery by the scaleni muscles. Placing the arm above the forehead may obliterate the pulse; Wright (1945) found that in over 80% of 150 young adults the pulse was obliterated when the arm was elevated in full abduction; the axillary artery is believed to be compressed or angulated over the root of the coracoid process or over the tendinous insertion of the pectoralis minor muscle. Cervical ribs have always to be borne in mind; the pulse is readily obliterated in such cases by posture. The anæsthetist must also remember that in some persons rotation of the head, or hyperextension of the neck, will lead to compression of the subclavian artery and loss of the distal pulse. In one of the thiopentone tragedies the injection of 4 ml. of a 10% solution was followed by extensive arterial thrombosis up to the axilla—the patient was in the Trendelenburg position at the time of the injection, and the anæsthetist rightly presumed at first that the posture rather than the injection was responsible for the absence of the radial pulse and for the effects in the hand. If thiopentone is injected into a non-pulsating artery, it will not only ascend to a high level but also will maintain its action undiluted. Hasler (1948) discusses some of the complications following such faulty posture in anæsthesia.

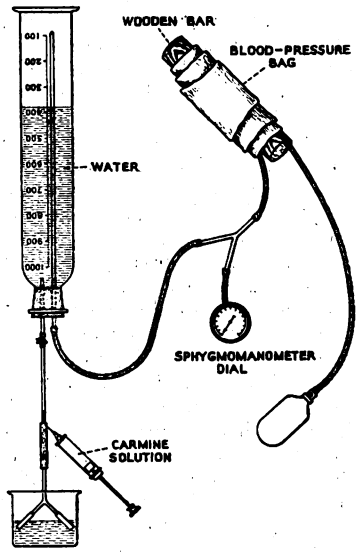


Fig. 3—Apparatus to mimic fluid flowing at arterial pressure and giving a flow of 30 ml. per min. in forearm: needle is introduced through rubber junction, carmine is injected with full force upwards through glass tube, and height of ascent of fluid is measured.

Pulse

The pulse has not always been closely observed in the affected limb; it may certainly remain full, and in two of the cases blood-pressure readings on palpation were the same in both radial arteries. The radial pulse has been found full for an hour and then disappeared; in one case the pulse was absent for an hour and returned only to disappear later. In three cases the full pulse gave a feeling of optimism, but pulsatian ceased some days later with alarming suddenness; in one, a child, it disappeared on the eighth day; in the second case the radial pulse disappeared on the tenth day, and section showed the vessel lumen lined with fibrin adherent to the intima but still patent; in the third case the radial pulse suddenly disappeared on the sixteenth day, and operation showed the brachial tree plugged with clot. The conclusion to be drawn is that the presence of a pulse does not exclude the possibility of severe damage to the intima and later precipitate thrombosis.

Fig. 2—Arteriograms: (a) full-force retrograde injection, showing height to which fluid ascended and enormous distension of arterial lumen; (b) slow injection, showing filling of arterial tree.

CLINICAL FEATURES

Pain

Intra-arterial thiopentone injection causes severe pain, coming on when about 2 ml. has been injected. The pain is agonising, and patients have described it as "like boiling water being poured over my hand," "a feeling as if my hand was on fire," "the hand felt like a flaming branch." On several occasions the complaint of pain during injection was regarded as due to the "patient's nervousness"; in one case the possibility of thiopentone being responsible for the postoperative pain was so completely overlooked that a neurologist's opinion was invited. He observed the thrombosed radial artery and indicated the cause. "Nervousness" on the part of the patient cannot be entirely dismissed as a contributory cause to the development of the more severe sequelæ.

Digitized by Google

Intense transient vasoconstriction, particularly of the distal arterioles, may follow and lead possibly to the trapping or the delay of some of the solution in the distal arterial tree. Wilkins et al. (1938) have shown that various stimuli, such as pinprick, taking a deep breath, or solving a mental problem, will temporarily decrease the blood-flow to the digits to as much as a twentieth of the previous level, independent of any alterations in systemic pressure. This does not happen with the sympathectomised limb and has some bearing on "post-accident" treatment.

Two of the patients (see below) developed shock after the intra-arterial injection, with poor pulse on the opposite limb also, and carpopedal spasm. This may be due to the pain, but severe vasomotor reactions have been described in arteriography with organic iodine compounds. Even intravenous solutions are not without risk, for intravenous pyelography, usually regarded as absolutely safe, has a mortality: Prendergrass et al. (1942) collected 26 deaths in 661,800 such examinations—an incidence of 0·0039%.

Idiosyncrasy or hypersensitivity to thiopentone has been described by Hunter (1943) and Hoenigsberger (1943) has recorded sudden collapse. I witnessed the sudden death, after an injection of thiopentone 0·5 g., of a perfectly healthy young soldier undergoing a minor finger operation. Necropsy did not reveal any cause, but in view of the vasomotor reactions with the intra-arterial injection it obviously becomes important to examine the forearm vessels in any such tragedies. Lundy (1942) declares "a certain number of fatalities are attributable to intra-arterial puncture"—though the immediate collapse makes it difficult to agree with the contention that death was due to "delayed return into the stream."

Area Affected

Six of the twelve cases ended with arm or forearm amputation; two with loss of fingers; two suffered severe nerve effects, with associated Volkmann's contracture of the interossei muscles of the thenar space in one case. The white hand—palm and dorsum—and the cyanosed fingers were early confirmatory signs of the accident. Such rapid cyanosis of the fingers, as Lewis (1936) has shown, does not indicate venous spasm or arrest, but implies a sluggish arterial circulation in a warm hand, leading to rapid reduction of oxyhæmoglobin. Some of the fingers soon became dark purple; these fingers ultimately suffered most. Others remained ashen grey.

Massive gangrene of the limb followed extensive thrombosis in the major vessels. Where these escaped, the ultimate damage depended on the direction of flow of the thiopentone; if this was swept into the muscles, the fingers were often spared. On anatomical grounds (see below)—and this is confirmed by clinical experience—inadvertent injection into the easily mistaken superficial ulnar artery is less likely to lead to the solution reaching and affecting the brachial artery bifurcation; the prognosis is thus better, for the entire limb blood-supply is not jeopardised.

Skin Patches

Several of the cases showed, besides the hand and finger involvement, mottled bluish-green patches in the skin of the forearm, round the elbow-joint, and in the arm well above the site of injection. Some of these patches merely blistered, being filled with clear or serosanguineous fluid; in other patches the skin died and sequestered, leaving punched sloughing ulcers.

Similar patches and ecchymotic areas have been observed in disasters consequent on arteriography. Lambret (1935) and Leclerc (1935) observed violet plaques, regarded as due to cutaneous and subcutaneous hæmorrhages, on the skin of the lower abdominal wall, following femoral arteriography; Leveuf (1935) and Wagner (1944) described this following the use of iodoxyl for brachial arteriography. The latter workers interpreted these patches as due to secondary spread of thrombosis from the main vessel to the distal cutaneous branches.

Thrombosis of the brachial artery can be excluded in the thiopentone cases, for in some with patches subsequent operation showed no such clot. These patches appear to be due to the direct local effect of the thiopentone solution shunted into the skin vessels. The work of Freudenthal (1924) favours this, for he showed that, in the patches of skin gangrene observed after the accidental injection of bismuth into a gluteal artery, the blocking of the cutaneous vessels by bismuth-salt crystals could be demonstrated by microscopy.

Limb Œdema, Muscle Death, Nerve Effects

A striking feature has been the extensive œdema of hand and forearm in some of the cases; this may be evident within two hours and well-marked within five hours, by which time it may have extended above the site of injection. When the forearm was explored, the muscles bulged on incision of the fascia but were of normal colour, and the œdema appeared not to have interfered with their blood-supply. Œdema of muscle appeared to be responsible for the flexion of the fingers in some of the cases, for it was noted that these could still be straightened passively. In one case such finger straightening became impossible at the end of six hours, the fingers being rigidly flexed and contracted—in a state of rigor mortis, like the Volkmann's ischæmic contracture of muscle. This is an important observation (Johnson 1946), for it confirms Lewis's opinion that muscle cannot withstand complete ischæmia lasting more than six hours. Dissection of three of the limbs after amputation showed the extensor muscles, as well as the flexor group, to be necrotic. This also is an important finding, for the extensor muscles have a good blood-supply through the profunda vessels, and one would expect these to survive, as they often do in the Volkmann contracture following trauma. It is likely, though we have no histological evidence for this, that the thiopentone solution spread into and thrombosed the dorsal interosseous artery on its extensor path as well, and thus blocked the linking distributing flow of the profunda vessels. It emphasises the need for a closer study of any such amputated arms.

Study of the extent of thrombosis of forearm vessels is also important, for it helps to explain the nerve effects in these cases. Adams (1942) has shown that the major nerves, as they traverse the forearm, receive branches of supply from the main arteries; interference with the blood-supply will interfere with nerve conduction (Holmes et al. 1944, Bentley and Schlapp 1943). The interosseous branch of the ulnar artery is particularly important in its blood-supply to the median nerve. These facts help to explain the anæsthesia and atrophy of the intrinsic muscles of the hand that developed in cases 4 and 8. Ischæmia of the nerve-trunks consequent on the arterial thrombosis, rather than the local action of thiopentone on the blood-supply of the muscles, seems here to have been responsible for the nerve lesions in the hand.

It is of some importance that œdema was never very conspicuous in these two cases, for Parkes (1945) has brought evidence to show that compression by œdema may be sufficient to arrest the blood-supply to the nerves and yet not affect pulse and nutrition in the distal part of the limb. His conclusions are based on the observations of Lewis et al. (1931), who have shown that nerves may be more readily rendered ischæmic because the blood-supply of their feeding branches can be obliterated by pressures as low as 60–70 mm. Hg. This work of Parkes indicates that, if the œdema after intra-arterial injection of thiopentone becomes severe, fascial

Digitized by Google

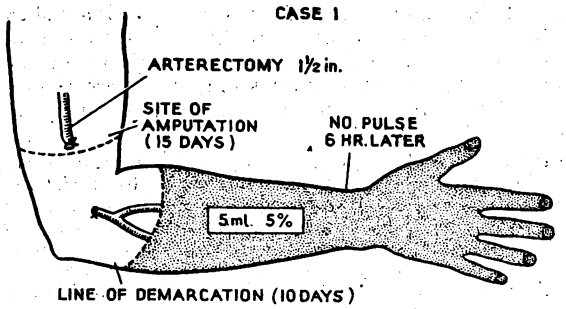


Fig. 4—Stippled areas in all figures indicate gangrene, unless otherwise indicated.

decompression by incision must be considered. The particular indication is a centripetal spread of the anæsthesia. Such fascial decompression was done in one of the cases with good result.

A further observation was that the fingers developing gangrene did not develop œdema; the fingers that recovered did. The absence of œdema indicates that the circulation in these fingers must have been completely arrested, that the major digital vessels were thrombosed. The fingers that recovered can have had spasm of the digital vessels only.

The march of events in the fingers after intra-arterial injection of thiopentone so closely mimics that of the "high-altitude frostbite" cases that were seen during the war that we turn to the beautiful studies by Davis et al. (1943) for comparative information about the pathology. They showed by capillary microscopy that there was either thrombosis or intense spasm in the distal arteriolar-capillary loops; such spasm might be maintained for twenty-four hours at least. When thrombosis had taken place in these digital vessels, no therapy was any good; and that applies to the thiopentone cases. An interesting observation, too, was that some of the "high-altitude frostbite" cases subsequently developed a "Raynaud's phenomenon" sensitivity to cold. One of the thiopentone cases that I examined several years after the injection had a similar complaint; a fact which may be of some medicolegal importance.

Loss of Consciousness

After intra-arterial injection of thiopentone, loss of consciousness was usually delayed, but apparently not more than 45–50 sec.; recovery of consciousness was rapid in several cases. With 3 ml. (5 or 10%) injected within 8 sec. unconsciousness usually followed within 20 sec. (Hunter 1947). Since total gangrene followed the intra-arterial injection of 4 ml. of 10% thiopentone and the patient lost consciousness, most of the solution must have passed through the arterial tree and could have been but momentarily trapped. The irritant action of thiopentone must therefore be immediate and powerful. This fact indicates that the intra-arterial injection of local antidotes—even if available—would be too late.

CASE-RECORDS

Case 1.—A soldier underwent excision of knee cartilage under low spinal anæsthesia, coöperating well. When tourniquet was applied he became restless and complained bitterly of pain. Skin was anæsthetic to forceps clipping, and operation continued. Patient, however, became agitated and apprehensive, tossing his head from side to side.

Injection of 5% thiopentone into right basilic vein at level of antecubital fossa was begun. Immediate complaint of pain at injection site. Since repeated aspiration did not show arterial blood, pain was attributed to patient's extreme apprehension. After 5 ml. he suddenly jerked his arm, and a large hæmatoma formed. Needle was removed, and cyclopropane anæsthesia continued.

Three hours later patient complained of considerable pain in antecubital fossa, and tingling sensation in right hand. Pain in antecubital fossa was attributed to interstitial spilling. Local heat was applied.

Six and a quarter hours after injection, fingers and wrist had become acutely flexed, and hand white and cold. Radial pulse absent, brachial artery pulsating just above elbow-joint but not below it. Entire hand and forearm completely anæsthetic.

On exploration brachial artery was found normal to 2 in. above bifurcation, then passed through a sausage-like tumour of extravasated blood. This was not tense, and further exposure of vessel showed also extravasation of blood into adventitia. Lumen was filled with thrombus to bifurcation and beyond.

Arterectomy.—1½ in. of brachial artery resected, and thrombus from radial and ulnar arteries extracted.

Postoperative Course.—Left hand and right leg immersed in water-bath at 112°F in attempt to force collateral circulation. Next day, some skin warmth on upper third of forearm, with sensation present to this point. "Spasm" of flexor muscles no longer present. Line of demarcation began to form, complete by eighth day; line extended from 4 in. below elbow on lateral side upwards to elbow-joint medially. Impossible to save joint. Amputation through arm on fifteenth day after injection (see fig. 4).

Extensive arterial thrombosis swiftly sealed the fate of the limb. The brachial artery can usually be ligated with impunity, if the collateral vessels are undamaged. It therefore appears that both the collateral branches and the main distal channels continued to be blocked by soft thrombus. Arterectomy certainly did not relieve so-called "collateral vessel reflex spasm"; the warmth of the skin of the upper forearm indicates that this could, in any event, never have been complete. The large periarterial hæmatoma is to be expected after arterial puncture, but is an unusual finding compared with other cases. A 5% solution is reported to have been used, which makes such a disastrous end-result unusual.

Case 2.—A soldier, aged 45, was operated on for depressed fracture of malar bone. A 10% solution of a "new thiobarbiturate closely related both clinically and pharmacologically to pentothal" was injected, exact amount not recorded. Immediate complaint of severe pain in hand and arm (notes report "solution was injected into an aberrant superficial ulnar artery").

A few seconds after injection, ulnar half of hand and ulnar border of forearm became fiery red. Reaction subsided

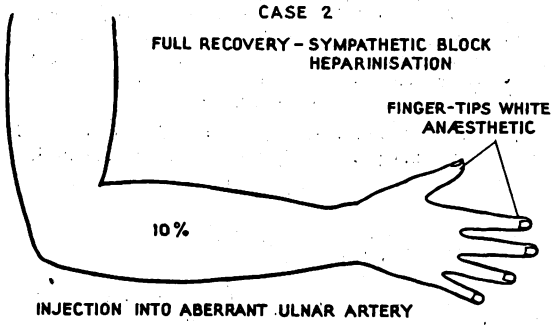


Fig. 5.

rapidly: replaced by mottled pallor. Immediate brachial-plexus block done ("satisfactory vasodilatation obtained"). Operation continued under cyclopropane anæsthesia.

At end of operation intravenous saline drip, containing heparin, started; both arms placed in hot-water baths, and patient packed with hot-water bottles. Some three hours after operation, hand again blanched, and tips of the third, fourth, and fifth fingers presented white patches; fingers felt numb to patient. On exposure, ulnar side of hand became distinctly colder than rest of hand and arm. Pulsation present in main arteries.

Sympathetic block of right stellate ganglion now done with 20 ml. of 2½% procaine hydrochloride in 1/1000 amethocaine; posterior approach used, and Horner's syndrome obtained. Much vasodilatation of right upper extremity followed, blanching of ulnar side of hand disappeared, and hand became warm.

Digitized by Google

Heparinisation continued; clotting-time, two hours after stellate block, 27 min. Patient now began to cough up considerable quantities of bright-red blood, which did not clot; apex of lung must have been injured during sympathetic block. Heparin stopped. Radiography showed nothing abnormal in chest.

Next morning, hæmoptysis had stopped, and clotting-time was normal. No further disturbances in hand.

Some fifteen days after original accident patient complained of dyspnœa on lying flat. Radiography showed large retro-pleural mass in relation to apex of right lung, extending posteriorly down to tenth intercostal space.

Aspiration produced 150 ml. of dark unclotted blood. Dyspnœa disappeared immediately, and hæmatoma was gradually absorbed (confirmed by radiography). (See fig. 5.)

The full vasodilatation that followed sympathetic block is an obvious pointer that this will be a useful measure in the management of such cases. Since the main vessels were pulsating fully thrombosis can be excluded, and the beneficial effects of the sympathetic block must be due to its effect in releasing spasm in the distal arterioles. Two further facts of significance are: (1) brachial-plexus block was as effective as the more difficult posterior sympathetic block; and (2) the arteriolar spasm recurred within four hours. Sympathetic block in a heparinised patient is well shown to be hazardous.

Case 3.—An adult, with gastric ulcer, admitted for partial gastrectomy was given heavy spinal 'Nupercaine,' followed by 4 ml. of 10% thiopentone and then nitrous oxide and oxygen. Injection reported as painful, hand became white, and on skin of forearm irregular blue patches developed. Radial pulse full and continued thus for whole day. Entire hand anæsthetic, as also distal half of ulnar aspect of forearm. Motor power poor: feeble finger flexion and extension possible; wrist could be held against gravity; but pronation and supination impossible. Flexion and extension of elbow good.

Next day circulation improving, pulse reported as "good," but forearm muscles firm and indurated. Circulation in fingers gradually improved.

On fifteenth day after injection, sudden loss of radial pulse; hand became cold and white, and finger and wrist movements impossible. Four days later mummification began. Oblique irregular line of demarcation developed in upper third of forearm.

Forearm amputation, thirty days after injection, made possible by dissecting out muscles, which were all avascular except for biceps and triceps; 2-in. bone stump was left. Ulnar and radial arteries and last 3 in. of brachial artery thrombosed. Normal pulsating segment not observed. Accompanying venæ comites not thrombosed. A useful small elbow stump saved (see fig. 6).

Particular features are: (1) only 4 ml. of a 10% solution was used; and (2) the radial pulse suddenly

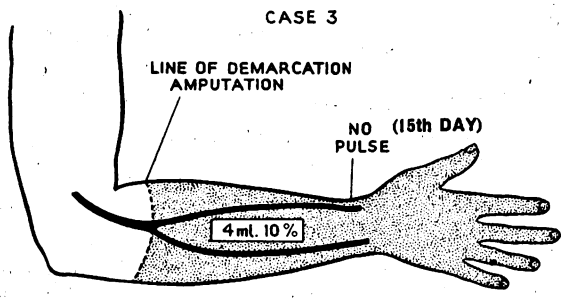


Fig. 6.

vanished on the fifteenth day. The loss of finger movement and the induration of the forearm muscles suggest that these were already dead before the final loss of the radial pulse. The onset of the late thrombosis is discussed below. A line of demarcation was waited for, and it is to be noted that there were no renal or other systemic effects from absorption of dead muscle tissue, as has been reported to follow arterial thrombosis with muscle death in the legs (Guthkelch 1943, Bywaters and Stead 1945). The saving of even a small elbow stump, by dissecting out the dead muscles, was an excellent manœuvre; for, contrary to the teaching of some surgical textbooks this small stump may prove of the utmost importance as regards the subsequent type of prosthesis (Gillis 1945).

Case 4.—A male, aged 22, admitted for mastoidectomy; 10% thiopentone used. "Vein in antecubital fossa, right arm, stood out well and felt superficial." Needle inserted over vessel, arm being fully extended. Piston withdrawn showed no blood; needle pushed on another $^1/_8$ in., piston withdrawn, and blood flowed freely into syringe; blood did not appear unduly red. Thiopentone 3 ml. injected fairly quickly; then pause; and, since patient was not sleepy, a further amount was given slowly.

In all about 8 ml. was given (last 2 ml. not injected). There was no difficulty in injecting and no swelling at site; patient did not complain of any pain or discomfort. The only thing noted was that patient took longer than usual before he became unconscious.

Taken into theatre, and airway inserted. He did not seem to like airway; nitrous oxide, ether, and oxygen continued, and intratracheal tube passed. Breathing became shallow, and patient appeared pale; head of table was lowered. On feeling for radial pulse, condition of hand was first noted. No pulse could be felt, though brachial pulse showed no

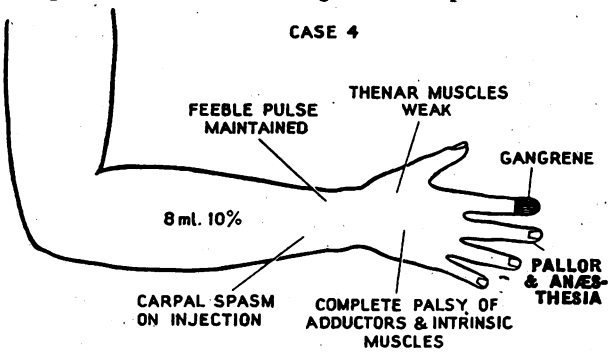


Fig. 7.

deterioration. Hand was in carpal spasm and white, with cyanotic patches. Nitrous oxide was reduced and oxygen increased; opposite arm was placed in hot water.

After about 10 min. muscular spasm relaxed a little, but still no improvement in colour of hand. Radial pulse had returned, but not so good as its fellow. At end of operation, radial pulse just palpable, colour of hand fair, but nails somewhat cyanosed.

On return to ward, unaffected arm was placed in a hot bath, 120°F, a hot cradle was applied to legs, and 150 mg. of nicotinic acid given by mouth.

Three hours after operation, both radial and ulnar pulses easily felt; but pallor and coldness of index and ring fingers continued—other fingers of good colour. Barbitone gr. 3, whisky 4 oz., and hot bath continued.

Nine hours after injection, pallor and coldness of ring and little fingers still present. Radial pulse just palpable, ulnar pulse "quite good." Pain (not severe) and numbness in fingers and thenar eminence. Patch of discoloration over anatomical snuff-box.

Ten hours after original injection, exploration of antecubital fossa under local anæsthesia. Difficult to define accurately the anatomy. Two small arteries with satellite veins were first encountered; pulsation was feeble; small segments of both vessels were removed. Deeper dissection now continued, and a further small parent artery strongly pulsating was seen (presumably brachial artery)—small segment excised.

At end of operation patient thought hand felt better. Hand was encased in wool; hot cradle to legs and immersion of opposite arm were continued.

Next day hand and fingers became swollen, all fingers now of good colour except tip of index finger, which alone was anæsthetic. Radial and ulnar pulses impalpable, but little complaint of pain. Nicotinic acid by mouth and papaverine three times a day continued.

Swelling of hand gradually subsided, movements of fingers became full, and colour of hand returned to normal except

Digitized by Google

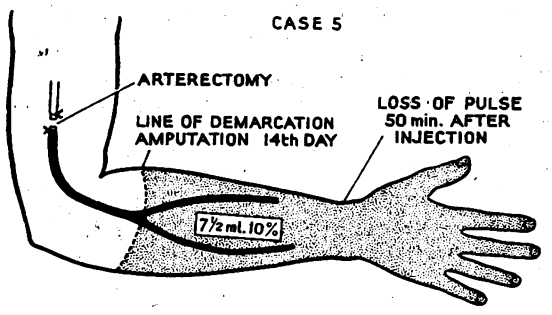


Fig. 8.

for discoloration of tip of index finger. Intrinsic muscles of hand appeared to be grossly affected, thenar muscles being weak, and interossei and adductors of thumb "apparently completely gone."

Further history of this case has been impossible to trace, but the anæsthetist informs me "he has heard that patient made complete recovery" (see fig. 7).

The loss of forearm pulses after the operation suggests that the patient had an arterectomy. After a brachial arterectomy the radial pulse usually returns within a few days (4 days as a rule). The non-return of the pulses indicates a continued blocking of the radial artery by soft thrombus; this is suggested too by the report of a good ulnar pulse before operation. The increasing anæsthesia of the hand suggests some post-operative extension of the thrombosis. The paresis of the intrinsic muscles of the hand and their later recovery indicate some blocking of the vascular supply of the main nerve-trunks. It might be suggested that the median nerve at the elbow received the thiopentone solution; but the entire hand was involved and the forearm muscles were not affected. We can only assume that the injection was intra-arterial, the complete absence of pain being unusual. The early muscle spasm suggests that much of the solution may have taken its path via the forearm muscles, and that may explain the fortunate happy result with such a large intra-arterial injection.

Case 5.—This case has been reported in detail by Johnson (1946). Male, aged 37, with buttock abscess. Needle entered into "median cephalic vein." Venous-looking blood aspirated, and injection of a 10% solution of pentothal begun. After 3·5 ml. "patient began to move about, this was taken to mean that he was tasting sulphur"; injection continued.

After about 7·5 ml. had been given, patient groaned and moved, but there was no indication of pain in the hand. Injection now stopped; patient lost consciousness; abscess incised. Anæsthetist noted area of petechial hæmorrhages about 3 in. broad above elbow, where nurse had compressed arm.

Recovery of consciousness apparently rapid—60–90 sec. Patient groaned and complained of pain in both arms, especially the left. Left hand was pale and bluish; both hands and feet went into typical carpopedal spasm. Both radial pulses present, equal, and of good volume. In the ward, 50 min. after operation, pulse had disappeared; forearm white and flaccid below elbow. (All spasm had disappeared from extremities.) Meanwhile, arm had been placed under electric cradle, and papaverine, carbachol, and alcohol administered.

No arterial pulsation below a point 3 in. above the elbow could be detected. Complete loss of voluntary movement in wrist and fingers, but passive movements full and painless, and such passive movement did not increase pain.

Six hours after injection, thumb had become flexed across palm, and fingers were beginning to contract. Static blood could be observed in capillaries; no evidence of capillary circulation. It was decided to explore the vessel, and this was done under general anæsthesia.

At a point 3 in. above site of injection brachial artery pulsation ended abruptly. Narrow band of demarcation well above site of injection. Below site of constriction vessel was slightly dilated and blue, obviously thrombosed.

Aspiration showed no fluid blood present. About 5 in. of artery was removed; it was filled with clot. No definite puncture site could be seen, nor was there staining or bleb in adventitia; no periarterial extravasation of blood. Patient was given heparin 10,000 units intravenously into other arm. Unsuccessful attempt to block cervical sympathetic by posterior approach.

Two days later some sensation had returned to upper third of forearm; skin here pink, but blue and sensationless below, indicating appearance of an early line of demarcation. Below this, arm showed all signs typical of dry gangrene.

Two weeks after original injection there was a well-formed line of demarcation extending $4^1/_2$ in. down radial side, and 3 in. on ulnar side, below elbow. Amputation eventually performed just above this level (see fig. 8).

Extensive arterial thrombosis was clearly the cause of limb death. The early maintenance of the pulse indicates that arterial spasm was not responsible for the thrombosis. Blistering at the site where the nurse had compressed the arm suggests that this may have been too vigorous, cut off the pulse, and permitted the higher injection of the solution. The onset of Volkmann's contracture six hours after the injection is valuable information; the previous painless passive movements possible indicate that the muscles before this time were still alive. Arterectomy made no difference to the ultimate result. In view of the carpopedal muscular spasms shortly after the injection, it is of interest to note that Macintosh and Heyworth (1943) reported that after an injection of 0·75 ml. of thiopentone into a cat's iliac arteries similar muscular contraction in all four limbs, of short duration, followed.

Case 6.—Female, 43, abdominoperineal operation. Given 10 ml. of thiopentone. "At the end of the operation the right arm was observed to be cold and pallid, as if arterial blood had been cut off." Thought possibly due to faulty position of arm on table. Both radial and ulnar pulses absent, and pulsation could be felt in brachial artery only high up—2 in.

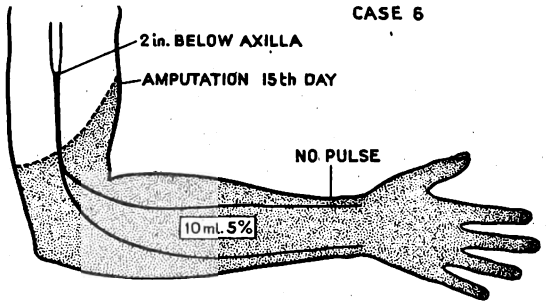


Fig. 9.

below axilla. "2% procaine was injected, in case this might be arterial spasm"; circulation did not improve.

Four hours after operation, cubital fossa was explored under local anæsthesia, and vessel was exposed from axilla to elbow. Brachial artery was anomalous, bifurcating about 1 in. above fossa; radial and ulnar arteries superficial, ulnar artery then disappeared beneath lacertus fibrosus to enter forearm.

Site of injection was clearly found in brachial artery, which was opened and found completely filled with clot; thrombosis extended from $1^1/_2$ in. below axilla far into forearm along the two branches. Those are the only operation notes.

Dry gangrene set in, fingers clawed, forearm became partially mummified, and a line of demarcation appeared extending from lateral side just above elbow round arm to 2 in. below axilla. Skin of upper arm looked healthy, presumably owing to circulation in profunda branch of brachial artery.

There being no urgent toxic symptoms, amputation was delayed until 15 days after original injection (see fig. 9).

A 5% solution of thiopentone was used; the resultant thrombosis was most extensive, blocking both the superior and inferior ulnar collateral vessels and leading to the formation of the line of demarcation above the

Digitized by Google

elbow. Such high thrombosis can only be explained on the assumption that the high Trendelenburg position, with consequent depression of the shoulder obliterated the pulse during the injection. The solution was thus injected into a non-pulsating vessel, and the high ascent of the solution and the sustained action of the thiopentone were thus made possible.

Case 7.—Man, 51, "highly strung," operation for hammer toe. Thiopentone 10% injected into a vessel on medial side of elbow. After 2 ml. patient indicated that he was "going off." A further 3 ml. then injected; patient now complained of severe pain in hand, saying "it feels as if on fire" and tried to vomit. Needle withdrawn and remaining 5 ml. injected into adjacent vein. Light gas-oxygen and ether continued.

Two hours later, patient looked very pale and was writhing in great pain. Hand cold, fingers ashen, dorsum of palm dead white. Patchy discoloration on ulnar border of arm. Both pulses present; equal blood-pressure readings. Superficial veins in forearm somewhat engorged. No hand œdema, no induration or swelling at elbow to suggest local leakage of thiopentone or blood.

Some two hours later, forearm was much swollen; muscles appeared to be under great tension. Wrist and fingers held

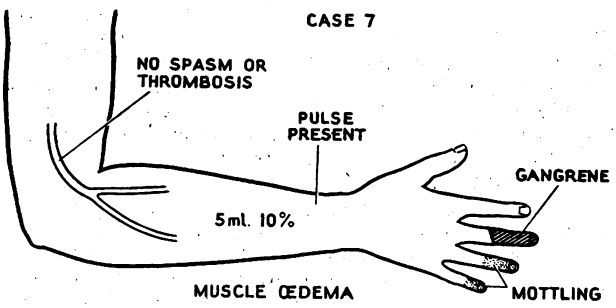


Fig. 10.

semi-flexed; attempts at active or passive movements caused acute pain. Engorgement of superficial veins more pronounced. Both radial pulses present; blood-pressure readings equal in both arms. Ulnar pulse could not be felt in either wrist. Tips of all fingers dusky and did not blanch on pressure. Palm and dorsum still deathly pale; no swelling distal to wrist. Pain of acute burning type, affecting diffusely all fingers and whole hand; patient in agony and unable to lie still.

Five hours after injection, swelling of forearm rapidly increasing, operation undertaken. Deep fascia incised from medial side of antecubital fossa to 3 in. above wrist. Immediate pronounced bulging of muscles, which were, however, of normal colour. Dissection showed that brachial artery branched high up in upper arm, and radial artery descended superficially just beneath deep fascia. Radial artery, dissected to middle third of forearm, showed strong pulsation throughout its length, with no indication of spasm or thrombosis. Ulnar artery similarly normal.

Circulation in thumb and index appeared to improve. Palm developed a mottled red flush, but dorsum unchanged. Reflex heating started. By next morning circulation of the index and thumb appeared normal; ring and little fingers were a mottled reddish-blue, but middle finger dark blue and very black as far as finger knuckle. Pain in hand easier, but in middle finger still intense.

Within 48 hours hand regained normal colour, except for terminal phalanx of middle finger and tip of ring finger. Middle finger still much discoloured; ring finger showing greyish-blue mottling. Movement and sensation had returned. Dorsum of hand and wrist had, however, become swollen, where previously not swollen; this may have been due to posture, for high elevation caused pain, which was relieved to some extent by horizontal or dependent position.

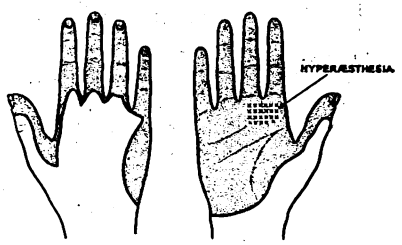


Fig. 12—Area of hypoæsthesia (stippled) in hand of case 8 fifteen months after intra-arterial thiopentone.

Ultimate outcome was loss of terminal phalanx of middle finger only (see fig. 10).

The successful issue in this case is first of all due to the skill and care of the surgeon (Mr. E. B. Jamieson, F.R.C.S.), whose very full notes I am able to relate, and who gave me the opportunity of seeing the patient. Secondly, the enormous muscle œdema appears to indicate that the pathway of most of the solution was fortunately via the forearm muscles; such pronounced early swelling of the forearm may thus be useful in attempting to assess the prognosis. The radial pulse was never lost, and the equal blood-pressure readings indicate that there could have been no spasm of a major vessel.

Case 8.—Male, 39, nephrectomy. Details of anæsthesia not available, but according to brief notes "after small pentothal injection there was complaint of pain; the needle therefore was withdrawn and injection continued into opposite arm." According to patient, immediately on injection he had agonising burning pain in the hand. When he awoke he had considerable pain, especially over thenar eminence. Possibility of thiopentone being responsible at that time not entertained.

Two days later, forearm was swollen, but "not the hand." There was "glove anæsthesia" of entire hand, feeble movement of fingers only possible, though wrist movements normal (fig. 11). Because of "glove anæsthesia" the patient was regarded as hysterical, and opinion of neurologist was sought, who noted absence of radial pulse and suggested that thiopentone had been injected into artery.

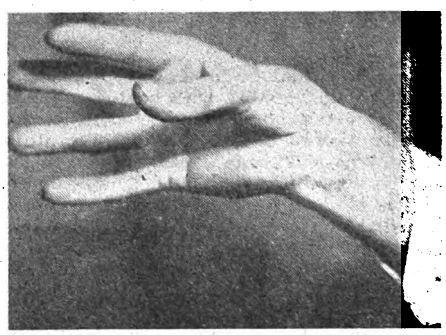


Fig. 13—Hand of case 8 two and a half years after intra-arterial thiopentone, showing adduction contracture of thumb following necrosis of thenar muscle.

When I first saw patient fifteen months after accident, he said he developed black and blue patches on forearm, which blistered. Healed scars were still present at my examination. Patient complained that he still had much pain at night, and hand felt as if skin was too tight ("like having on a too tight pair of gloves"). There was hypoæsthesia of entire hand, with a small patch of hyperæsthesia in palm (fig. 12). Thumb held in tight adduction (fig. 13), and muscles of thenar interspace and abductor pollicis felt woody hard. Finger movements now full, but fingers showed wasting of pulp, loss of transverse skin ridging, and distorted nail growth; they were warm. Radial pulse absent, and vessel could be traced upwards as a thrombosed cord.

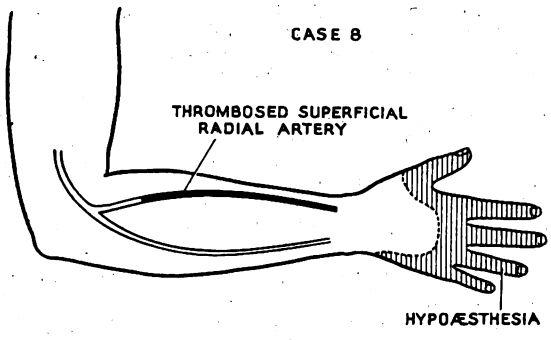


Fig. 11.

Digitized by Google

Later, some of contracted muscle mass was excised by his surgeon; section showed complete muscle necrosis (fig. 14).

I again saw this patient some $2\frac{1}{2}$ years after original injection. He then complained that with cold the fingers went a dirty grey, movements became difficult, and finger numbness prevented him from using hand. On any heavy work hand went dead white.

The fingers do not appear to have been affected, except for later secondary effects; this suggests that the thiopentone was embolised in the main to the forearm muscles and thenar space. Death of the muscles of the thenar space indicates that the radial artery must have been responsible for most of the supply, and that spread of the thrombosis along this vessel into the distributing branches blocked the ulnar-artery anastomosis. This is very much akin to the march of events with an arterial embolus, distal clot blocking the collateral vessel path. The hand anæsthesia, which apparently took well over

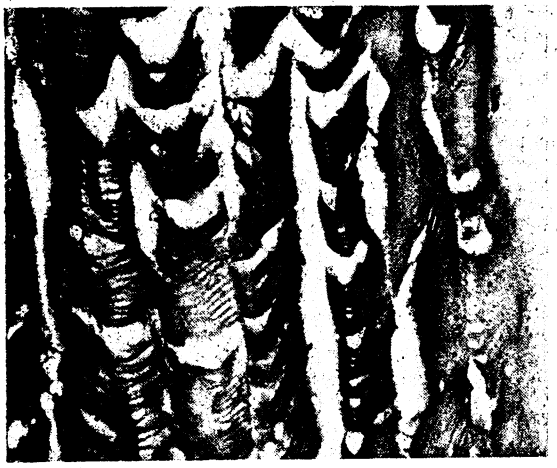


Fig. 14—Biopsy specimen showing coagulation necrosis of thenar muscle in case 8.

18 months to recover, has two possible explanations: (1) forearm œdema, with compression of the vascular supply of the nerve-trunks (the œdema was, however, never very extensive); and (2) spasm or thrombosis of the vessels of supply to the medial and ulnar nerves. The loss of power in all the intrinsic muscles of the hand suggests the latter ætiology—ischæmia of the main nerve-trunks. The "Raynaud's phenomenon" sensitivity to cold is an interesting observation which has not been encountered in any of the other cases. There has, however, been no opportunity for the late examination of the recovered patients.

Case 9.—Male, 52, with prolapsed iris. Anæsthesia induced with thiopentone, 10% solution. The "vein" was superficial and easily entered on the first attempt. After 4 ml. complaint of severe pain in arm—"you're breaking my arm." Aspiration showed free blood-flow, injection continued. Noted "he took a little longer to go under than usual."

On recovery from anæsthetic, pain in arm was first thing complained of. Nothing abnormal noted. Some 4 hours later, thumb and index finger were whiter than rest of hand, and a bulla $\frac{1}{2}$ in. in diameter, filled with clear fluid, had appeared on thenar eminence.

Next morning, thumb and index finger dusky, and patient had severe pain in forearm and a "sensation as of tight band" round distal phalangeal joints of thumb and index finger.

By evening, distal phalanges were dark purplish-black, fading to dusky grey over second phalanx. On thumb, discoloration extended farther on palmar aspect than on dorsum, reaching thenar eminence, where there was purplish-yellow blotchy discoloration. Hand and forearm were much swollen up to elbow. Generalised erythema of forearm, œdematous area being slightly warmer than on other side. Thumb and index phalanges anæsthetic and cold to touch.

Forty-eight hours after injection, irregular patches were present over forearm, largest being over radial border. These

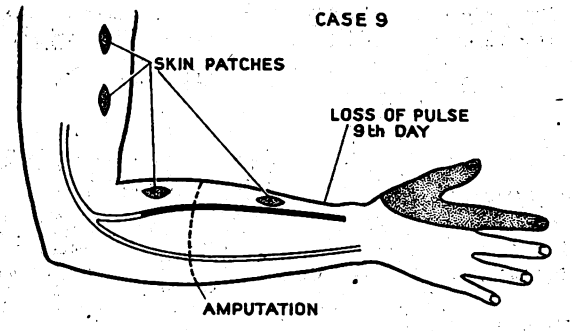


Fig. 15.

patches later developed purplish central area. Radial pulse felt normal and arterial wall in "good condition."

Hand continued thus for 5 days; thumb and index finger then became black and gangrenous, and skin patches on forearm began to slough.

Nine days after injection, radial pulse, which had remained normal, "suddenly" disappeared. Cubital fossa was therefore explored under brachial-plexus anæsthesia. Basilic vein found thrombosed. Radial artery thread-like and did not pulsate; ulnar branch pulsating.

Brachial artery was then explored; its pulsations were normal, and vessel was opened to extract any clot. Intima appeared normal, no clot was found, and vessel was resutured. One inch of radial artery was resected; there was no return bleeding from distal end.

Microscopical examination showed intimal swelling and fibrin filling vessel lumen, but channel still present.

Some 6 weeks after injection, thumb and index were amputated. Unfortunately infection supervened, and final amputation had to be performed through forearm some 3 months after original accident (see figs. 15–17).

The original injection was probably in the brachial artery, but it seems that most of the thiopentone spent itself, via the radial artery, in the thumb and index finger. The disappearance of the pulse on the ninth day is not easy to explain, since the vessel was filled with fibrin rather than with clot, a finding to be expected usually where there has been long-continued vascular spasm. Microscopy showed considerable swelling and damage of the intima, which confirms that this vessel carried the brunt of the solution. The sloughing skin patches above and below the site of injection appeared to be due to local effects of thiopentone. An explanation of the high distribution of some of the skin patches on the arm has already been attempted. It is clear

Fig. 16—Gangrenous segment of hand amputated six weeks after intra-arterial thiopentone (case 9).

that there was thrombosis, at an early stage, of the digital vessels of the thumb and index, for these fingers never became swollen, indicating complete arterial arrest. The finding of a thrombosed cubital vein suggests that this may have been traversed to reach the artery.

Case 10.—This case has been reported by Macintosh and Heyworth (1943).

Patient was given 5 ml. of 10% thiopentone into an aberrant ulnar artery.

Thin rubber venous tourniquet and "best-looking vessel" selected. No. 17 needle, blood aspirated, and injection begun at moderate speed. After 5–10 sec. patient complained of very severe pain in whole hand, as "though boiling water

Digitized by Google

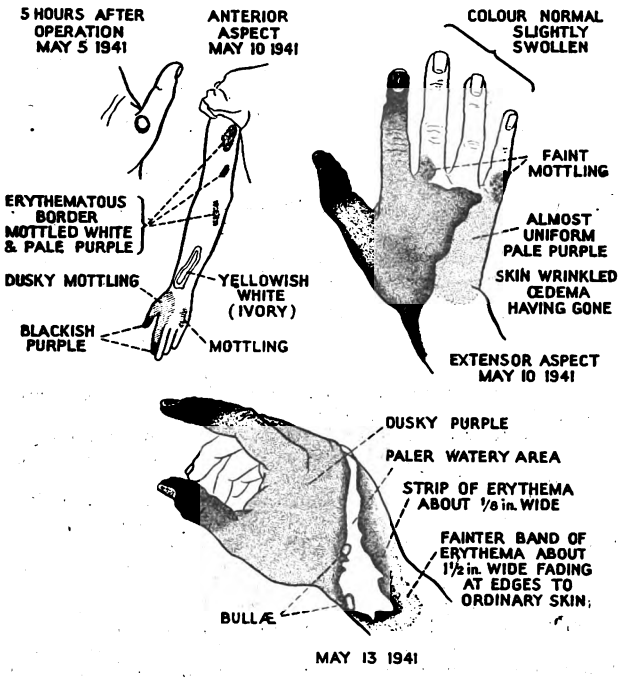


Fig. 17—March of events in case 9: hand and forearm during first week after intra-arterial thiopentone.

was being poured on it, and flames shooting from ends of fingers."

Injection stopped and "vessel" found swollen to size of a lead pencil, hard, and pulseless for about 4 in. distally—i.e., in its superficial course. Patient went grey and started sweating; about 45 sec. later lost consciousness. Anæsthesia continued with nitrous oxide and oxygen.

Some 5 min. later, ulnar three fingers and hypothenar eminence cold and blanched. This lasted $^1/_2$–$^3/_4$ hour; 15 min. after injection, mottled purple and red purpuric rash developed on lower part of ulnar aspect of forearm, and spread to hypothenar eminence. This lasted about five days.

After operation patient woke with very severe pain in hands; morphine necessary. Next morning moderate œdema of whole hand and wrist. Artery hard, but not so swollen as immediately after injection.

Ten days later, patient symptomless but remained with a thrombosed aberrant ulnar artery. Similar aberrant vessel on opposite arm (see fig. 18).

The ultimate effect of this injection of 10% thiopentone was indeed fortunate; some gangrene of the fingers at least was to be expected. An immediate thrombosis appears to have followed the injection, and this was also observed in Van der Post's (1942) case (case 12). Serious sequelæ are less likely after puncture of an aberrant ulnar artery (see anatomical explanation below). The vessel in case 10 pursued a subcutaneous course and pierced the deep fascia in the distal part of the forearm.

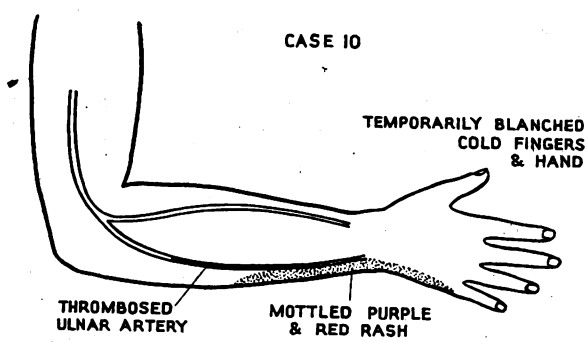


Fig. 18.

The blanching of the fingers, lasting only $^1/_2$–$^3/_4$ hour, must imply that there was only temporary spasm of the vessels. The character of the pain indicates that the injection was certainly intra-arterial, and the fact that all the finger-tips were affected indicates a fairly wide distribution of the thiopentone. Why there were no ill effects I cannot explain.

Case 11.—This case has also been reported by Macintosh and Heyworth (1943).

A boy, aged 5 years, was given 1·5 ml. of 10% thiopentone as induction before tonsillectomy. An hour later, child complained of severe pain in hand and distal part of forearm, which was blanched from elbow downwards. In about an hour colour returned, pain appeared to pass off, and child went to sleep. Discharged from hospital two days later.

Readmitted a week later because of sudden severe pain in forearm. According to parents, child had continued to complain of pain in right arm from date of discharge; pain prevented him from sleeping. As time went on, pain in wrist seemed to increase, and a blue mark in middle of right elbow and several black marks on ulnar aspect of forearm were noted.

Hand and arm were warm and of good colour. Child kept forearm and wrist bent and could not move them. Three days later, hand had improved; child managed to turn over leaves of his book but could not hold anything in right hand. Five days after injection, child appeared to be free from pain, played, and moved his hand.

On *eighth day* he complained that arm was again painful and stiff. He went out to play but came back screaming with pain; hand white, nails blue.

In hospital, hand was ischæmic, cold, with blue nails. Forearm was held in semi-flexion, and wrist in palmar flexion; fingers were tender on attempting dorsal flexion. Strong pulsation could be felt in brachial artery up to middle of elbow, where it suddenly ceased. No radial pulse. Hand was anæsthetic as far as middle of hand, though such sensation could not be determined accurately in a child. There were a few

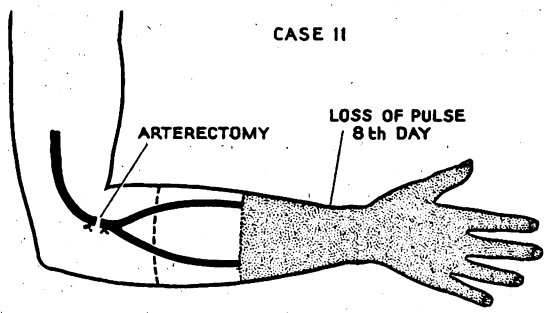


Fig. 19—Broken line indicates site of amputation.

bluish spots in middle of forearm, and there was a dark area over injection site.

Observation continued for two days, during which there appeared to be recurrent spasms of pain in wrist. No movement was possible in fingers, hand remained cold, and sensory loss appeared to be extending upwards.

Ten days after original injection, elbow was explored. Brachial artery was pulsating throughout antecubital fossa, but no pulsation could be seen in its divisions. Radial artery was so blue that it was first mistaken for venæ comites. After a temporary clamp had been placed on brachial artery, radial artery was divided 0·5 cm. from its origin. Lumen was found filled with old dark blood-clot, which appeared to extend entire visible distance of radial artery—4 cm. On removal of clot from proximal end, vessel began to bleed slowly, and this end was therefore ligated. Entire brachial-vessel division was now exposed; ulnar artery was swollen, glossy, and soft, with doubtful pulsation. Brachial artery appeared swollen ("abnormal bulge") in terminal 1·5 cm., and it was decided to resect this section of brachial artery up to its bifurcations. Heparin injected into ulnar and radial arteries, but very little flowed down. Finally entire visible length of radial artery, which contained clot throughout was resected. Portion of radial artery which was handled was smaller than unhandled portion, even though clot extended throughout.

Digitized by Google

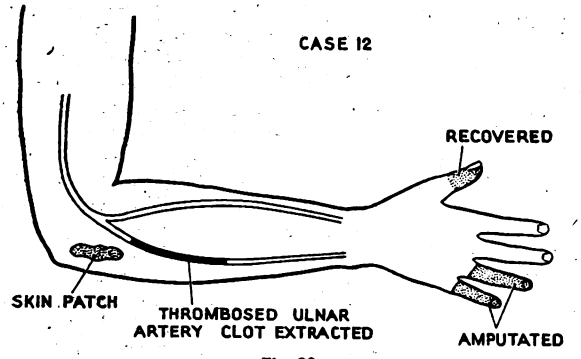


Fig. 20.

Pathologist's Report.—Brachial artery: some endothelial thickening of wall and a little fibrin deposited deep to endothelium.

Radial artery (3 cm. long by 2 mm. broad): endothelial proliferation, and at one point a small mass of fibrin which was clearly present before removal. Rest of arterial lumen occupied by unorganised blood.

Muscle: a small piece, taken at operation, "shows early degenerate changes, with loss of cross-striation and some abnormality of staining. There are also places with proliferation of sarcolemmal cells. These degenerative changes are much slighter than has been observed in other ischæmic muscle."

After operation, hand became discoloured to middle of forearm, and cold. Three weeks after exploration a forearm amputation was done, leaving a $2^1/_2$ in. stump. Pathologist reported "no thrombi in distal smaller arterials," and considered that "obliteration responsible for death of limb took place at some point above site of amputation" (see fig. 19).

Recurring spasms of pain, like those the child had after discharge from hospital, are often noted in limbs with severe ischæmia. The sudden attack of pain a week later must indicate an extension of the thrombosis. The child was playing at the time; experience with arterial disease shows that, in a thrombotic lesion, extension of the level of thrombosis may sometimes be precipitated by exercise. Late thrombosis on the eighth day is often seen with venous thrombosis—e.g., in the leg. Wright (1947) has demonstrated that about that time after operation there is an increase both in number and in "stickiness" of the platelets, and this may be a responsible factor in the late thrombosis in the thiopentone cases. Arterectomy certainly did not relieve the condition; the value of this procedure, in the light of experience with other cases, is discussed below.

Case 12.—Reported by C. W. H. Van der Post (1942). Given in all 6 ml. of 10% thiopentone for dilatation and curettage. Puncture was difficult. After injection of 1 ml. an immediate red flush spread down arm, and "whole vein down arm was thrombosed." Operation was successfully completed.

Next day, terminal phalanx of thumb and two fingers "were going gangrenous." Arm œdematous to just above elbow, and little and ring fingers insensible to touch and temperature; terminal phalanx of thumb cyanosed, with one or two bullæ in skin. Radial pulse was palpable, and ulnar artery could be palpated only as far as elbow. Bluish-green patch round inner aspect of elbow.

Surgeon explored elbow under general anæsthesia and found an anomalous origin of ulnar artery, which arose from brachial artery a full inch above elbow and then passed superficially to flexors of forearm. Ulnar artery was opened just above elbow, and thrombus about $^3/_4$ in. long and $^1/_8$ in. thick was extracted; vessel incision was sutured.

Next day, some improvement of arm, fingers becoming warm, and sensation returned. Convalescence interrupted by severe uterine hæmorrhage. Finally terminal phalanges of ring and little fingers were lost, whereas thumb recovered (see fig 20).

Injection was into the easily mistaken superficial ulnar artery. Arteriotomy, with extraction of the clot, seems to have been valuable, for the ultimate result can be regarded as satisfactory. The immediate formation of thrombus fits in very well with the march of events in case 10. It must be remembered that severe hæmorrhage, as in case 12, leads to intense vasoconstriction and will influence the recovery of the ischæmic limb. The involvement of the thumb shows that, despite the ulnar-artery puncture, the thiopentone was widely distributed. There is the less likely alternative explanation that, if the brachial-vessel division was very low, some of the thiopentone may have been injected in retrograde manner into the brachial artery and then distributed via the radial artery.

Other Cases.—I have had personal communications from at least six other anæsthetists who believe that they have injected 5% thiopentone intra-arterially with no subsequent effect except for a flushing of the limb. I have seen one case after such injection and noted the flushing of the limb and that there was not the slightest sign of extravasation of blood to suggest that the artery had been punctured. This patient had a particularly mobile elbow, and on hyperextension the brachial artery came well forward, was tightly stretched, and invited injection. Lundy (1942) has reported the intra-arterial injection of 8 ml. of $2^1/_2$% thiopentone in 2 cases, with no untoward effect. Adams (1944) reports injection of 5 ml. of 10% thiopentone with no near or remote effect, which is indeed surprising. Lees (1943) has reported a case where, after an injection of 5% thiopentone there followed burning pain and a spreading red flush down the forearm; he felt sure that the injection was "intravenous," but the story is typical of intra-arterial injection.

(To be concluded)

TRANSORBITAL LEUCOTOMY *

WALTER FREEMAN
M.D., Ph.D. Washington, D.C.
From the Department of Neurology and Neurological Surgery, George Washington University School of Medicine

LESS than a year after the introduction of leucotomy by Moniz (1936), Fiamberti (1937) proposed a simplified operation, which later he carried out, on the frontal lobes by way of the orbital plate. This route had been used before for certain intracranial procedures such as ventricular puncture (Dogliotti) and intracerebral malaria inoculation (Ducosté) with ease and safety. Fiamberti insisted on these aspects, but did not compare the effectiveness of the method with that of other types of leucotomy. Then the war prevented further communications, and only in 1947 did Fiamberti's work again come to notice outside Italy. The results were still not very substantial, and the papers by Fiamberti (1947), Ali (1941), and Ferraro (1942) gave no clear idea of the virtues of this approach, merely denying its vices. In justifying his novel approach Fiamberti stated: "In the present state of affairs, if some are critical about the lack of caution in therapy, it is, on the other hand, deplorable and inexcusable to remain apathetic, with folded hands, content with learned lucubrations upon symptomatologic minutiæ or upon psychopathic curiosities, or, even worse, not even doing that." In a recent personal communication Fiamberti writes that he has performed about 100 of these operations without mishap, but he is still indefinite about the results.

Two important pieces of research, the results of which have not yet been published, call attention to the possibilities of transorbital leucotomy as a valuable addition to the therapeutic armamentarium of the

* A paper read at the Burden Neurological Institute on July 11, 1948.

Digitized by Google

psychiatrist. One of these, by the Columbia-Greystone associates, reported at the New York Academy of Medicine in April, 1948, indicated that the favourable results obtained with frontal leucotomy may be duplicated by excision of the cortex covering the frontal poles of the brain, and in particular those parts termed areas 9 and 10 on the Brodmann chart. Furthermore, the investigators claimed that the changes in personality following "topectomy" are much less severe than those following leucotomy. The series of cases is rather small (24) and the period of postoperative observation has been rather short for assessment of final results, but of the 11 carefully selected patients in whom areas 9 and 10 (and part of 46) were excised 10 were usefully occupied after discharge from hospital.

The other investigation, by Spiegel and Wycis and their collaborators, reported at the meeting of the American Neurological Association in June, 1948, involves a direct attack on the medial nucleus of the thalamus with a stereotaxic instrument based upon the Horsley-Clarke apparatus. After the electrocoagulation of 3–5 minute areas in each medial thalamic nucleus patients are said to develop disorientation, incontinence, masking of the face, plateau speech, and abolition of the emotional component of the psychosis. Clinical improvement is comparable with that observed after leucotomy. This research bears out the theory of Freeman and Watts (1947) that the affective change in the patient is due not so much to interference with the cerebral cortex as to the retrograde atrophy that affects the thalamus once its connexions with the cortex have been severed. The topectomy investigation indicates that a more restricted operation on the frontal lobes may successfully relieve the patient without producing a serious change in personality.

Consequently, transorbital leucotomy, which undercuts areas 9 and 10, seems to be a valid procedure.

Our own studies on the cadaver in 1945 confirmed the fact that the orbital plate could be rather easily perforated without danger to structures within the orbit and without encountering large intracranial vessels; and that the thalamofrontal radiation could be severed fairly far anteriorly without disturbing the cortex except to a minimal degree.

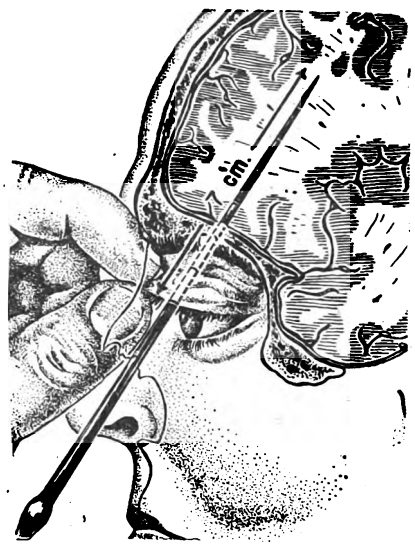
Early in 1946 10 patients were subjected to transorbital leucotomy with encouraging results. Two years later (Freeman 1948) 6 of them were fully restored and only 1 was in hospital. The series has been extended since then to more than 100 cases, in collaboration with doctors in mental hospitals in South Dakota, West Virginia, California, and the State of Washington (Jones and Shanklin 1948). There have been no deaths.

TECHNIQUE

We have found that transorbital leucotomy can be performed satisfactorily in the postconvulsive phase of electro-shock. Electro-shock appears to have a generally disrupting effect on cortical activity, temporarily abolishing the psychotic manifestations and bringing the patient into a brief period of increased adaptability. When leucotomy is also performed, the effects of the electro-shock seem to be at least protracted, and often permanent. A few operations under ordinary anæsthesia have been performed by others, however, and equivalent results are reported. Nevertheless, electro-shock requires so little preparation and is so familiar to the psychiatrist that it seems to be the method of choice.

To maintain the patient in a somewhat prolonged phase of coma, two convulsive doses of electricity are given, the second about one or two minutes after the first convulsion has subsided. After the second convulsion a towel is placed over the patient's nose and mouth to prevent contamination by saliva and nasal secretions. The upper eyelid of the patient is pinched between thumb and finger, bringing it away from the eyeball. The point of the transorbital leucotome is then introduced into the conjunctival sac and moved around against the roof of the orbit until the top of the vault is encountered. The leucotome is brought parallel with the bony ridge of the nose, and its base is tapped lightly with a hammer to drive it through the orbital plate. To aim the leucotome properly the shaft must press rather strongly on the eyeball, but no harm to the globe has been noted except for occasional subscleral hæmorrhage.

The transorbital leucotome† consists of a tool-steel shaft 12 cm. long and 4 mm. in diameter, tapering for the last 6 cm. to a rather fine point with a slight bevel. Its handle is 7 cm. long and 8 mm. in diameter and equipped with a cross-arm at the base. The shaft is graduated in centimetres, a double line being marked at 7 cm. which is the most frequently used point.



Transorbital leucotomy.

When the leucotome has reached the 4 cm. level, its handle is pushed laterally as far as the margins of the orbit will permit to sever the fibres in the lower portion of the thalamofrontal radiation. It is again returned to mid-position and gently driven to a depth of 7 cm. always in the plane of the bony ridge of the nose (see figure). At this depth it is possible, by swinging too far, to lacerate arteries in the depth of fissures on either the medial or the lateral surface of the frontal lobe; and, since the thalamofrontal radiation is a rather narrow band in this region, a movement of only 15–20° laterally and medially is sufficient. When the sweeps of the instrument have been made, it is withdrawn, and moderate pressure is maintained over the eyelids for several minutes to prevent excessive bleeding into the orbit.

Unless the patient is still deeply unconscious, an additional electroconvulsive shock should be administered before the other side is operated on. Patients seem to tolerate multiple convulsions quite well. In view of the refractory period, it is usually necessary to increase the time of passage of the electric current by repeated tripping of the switch until the convulsive threshold is reached. No complications have been encountered in doing this. After the convulsion has subsided, the other side is operated on in the same way.

Recovery from transorbital leucotomy can be very rapid. Sometimes within an hour the patient may be awake and talking. Headache is usually present, and occasionally nausea; incontinence is rare. Swelling of the eyelids is common but tends to clear in a day or two. Ecchymosis is often encountered, and the discoloration may persist for two weeks. The swelling is probably due to the escape of cerebrospinal fluid through the orbital plate. Rhinorrhœa has not been observed. Complications have developed in only 3 of more than 100 operations. In all of these there was bleeding, with very severe inertia and paralysis in one, and mild hemiparesis in the others.

† Made by H. A. Ator, 5332–29th Street, N.W., Washington, D.C.

Digitized by Google

All three patients recovered and went home, but their usefulness is limited.

RESULTS

General and undesirable changes in personality after transorbital leucotomy are usually minimal. Only occasionally is there a certain indolence and tactlessness. For the most part the patients are quite themselves, the only thing lacking being a certain subtlety and a modicum of insight into their own mental mechanisms. Personality tests by Dr. Mary Frances Robinson have revealed richness as well as depth in patients who have been operated on by the transorbital route.

Return to effective existence may also be rapid. Some patients who have been under maintenance shock-therapy on an ambulatory basis have left the hospital on the day following operation and have been back at their household tasks within a week. Others have returned to their positions as soon as their black eyes have cleared. Three patients have been married since operation and are reported to be carrying on normally.

Response to operation is of course variable, depending in part on the previous personality and the type and severity of the illness. Sometimes there is a spectacular response; more often there is a period of elation followed by a return of symptoms and then slower and more steady improvement. Sometimes patients only maintain these improvements for a period and then relapse. The worst patients, especially among schizophrenics, show little change, but they may be benefited later by major frontal leucotomy. Transorbital leucotomy can render patients more responsive to other forms of treatment, particularly electro-shock therapy. Perhaps the greatest change observed in patients is their increased friendliness and sociability when their emotional tensions have been lifted. Thus effective psychotherapy may become possible for the first time.

Certain symptoms of mental illness are helped, and others not. Anxiety and emotional tension, for instance, are often overcome; depressive ideas, phobias, and obsessional thoughts usually improve. Fixed delusions and hallucinations are rather resistant, and motor compulsions or tics may continue relatively unchanged. If operation is performed before the psychosis or neurosis becomes fixed, however, even the most ominous symptoms may subside within a few days.

INDICATIONS AND CONTRA-INDICATIONS

Transorbital leucotomy perhaps finds its most successful application in certain patients who improve and then relapse or who are being carried on maintenance shock-therapy. This applies particularly to schizophrenics who have been in hospital for many months and have not recovered with shock but are not yet too emotionally deteriorated to benefit from leucotomy. Patients with depression of middle and later life, particularly the anxious types, may do well with transorbital leucotomy after the failure of shock therapy. Obsessionals and patients with anxiety states, hypochondriasis, and psychosomatic conditions have been helped within the general limitations reported above. Thus far, patients with intractable pain of long duration have not responded as well as to major leucotomy (Freeman and Watts 1946). Schizophrenic psychosis of long duration is generally a contra-indication, though reports from certain hospitals indicate that disturbed behaviour may be brought at least partly under control. Severe emotional dilapidation is the outstanding contra-indication to leucotomy of any type, and can certainly not be overcome by the transorbital operation. We have not yet had any experience of its use among alcoholics, drug addicts, or criminals.

Transorbital leucotomy has proved valuable in mental hospitals where specialised neurosurgical techniques are rarely available. It is also applicable in patients who are not recovering but nevertheless do not seem to be sick enough to require major leucotomy. The operation can be performed by the psychiatrist as soon as he has familiarised himself with the landmarks and practised on the cadaver. It requires little more preparation of the patient than is demanded for electro-shock therapy; the operation is brief, safe and simple. Even the route of approach to the brain requires no preparation, since the conjunctival sac is normally sterile and a copious flow of tears is promoted by the electric current. No complications due to infection have been reported, but sulphadiazine 4 g. in divided doses is given as a routine after operation.

At the Washington meeting of the American Psychiatric Association on May 19, 1948, where this work was first reported in the U.S.A., speakers from half a dozen different hospitals emphasised the safety and effectiveness of transorbital leucotomy. One-third of the schizophrenics and more than half the involutionals treated had been discharged. Further follow-up studies and work will be needed to determine the lasting value of the method and to learn more about its indications and contra-indications compared with major lobotomy; but it seems promising at present.

SUMMARY

Frontal leucotomy can be performed safely and effectively by the transorbital route of Fiamberti during the phase of coma following electro-shock.

Recovery may be very rapid and undesirable changes in personality are minimal.

The operation is a minor one and may be performed by the psychiatrist provided he has thoroughly familiarised himself with the technique and landmarks through previous practice on the cadaver.

The operation has been most effective in certain patients where tension was a prominent feature of the illness and who were beginning to become chronic in spite of more conservative therapies.

I wish to acknowledge the assistance of my widely scattered colleagues: Drs. Haas and Williams, of Yankton, South Dakota; Drs. Keller, C. H. Jones, and J. G. Shanklin, of Fort Steilacoom, Washington; Dr. R. B. Toller, of Stockton, Calif.; Dr. E. H. Reaser, of Huntington, West Virginia; and Dr. Joseph Knapp, of Weston, West Virginia.

REFERENCES

Ali, V. (1941) *Neopsichiat.* **7**, 1.
Ferraro, M. (1942) *Note Psichiat., Pesaro*, **71**, 1.
Fiamberti, A. M. (1937) *Rass. Studi psichiat.* **26**, 797.
— (1947) *Rass. Neuropsichiat.* **1**, 3.
Freeman, W. (1948) *Med. Ann. Dist. Columbia*, **17**, 257.
— Watts, J. W. (1946) *Lancet*, **1**, 953.
— — (1947) *J. comp. Neurol.* **86**, 65.
Jones, C. H., Shanklin, J. G. (1948) *Northw. Med., Seattle*, **47**, 421.
Moniz, E. (1946) Tentatives opératoires dans le traitement de certaines psychoses. Paris.

"... The world of the future—if any world survives—will be a world of diversity, held together by a conception of common interests. It will be a world in which many political faiths and economic creeds are tolerated and widely differing points of view fertilise each other for the common good. Our challenge in this generation is to discover the common interests, the terrain of possible collaboration, the overlapping areas of curiosity and sympathy, of aspiration and mutual advantage, that bind the human race together regardless of ideologies or boundary lines. The search for these rallying points of unity, the development of new techniques and areas of coöperative action where ideas and experience can be pooled and combined—this is the immediate task; this comes first; this is the foundation of the ultimate structure of a united society.... In spite of all evidence to the contrary the things that divide the world are trivial as compared with the things that unite it. The mutualities of human beings everywhere far exceed their divergencies."—Dr. RAYMOND B. FOSDICK in the *Rockefeller Foundation Review* for 1947.

Digitized by Google

INCONTINENCE OF URINE IN THE AGED

THOMAS S. WILSON
M.D. Belf.
GERIATRICIAN, CORNWALL COUNTY COUNCIL

INCONTINENCE of urine has long been recognised as particularly likely to occur at either extremity of life. Allen (1733), quoting the "Sentiments of Ettmüller—Of an Incontinency of Urine," states:

> "The Cause of an involuntary discharge of Urine, is a Deficiency in the Constriction of the Sphincter of the Bladder, by a Palsy, Contusion, by staying too long in cold Water, by a difficult Labour, and sometimes it happens to Women in the last months of their going with Child. . . . Children and Old People are the common Pissers-a-bed, but these come not to the Physician for Cure."

Allen does not give the reason for this attitude of therapeutic negativism, though he later says: "in old Persons it is altogether incurable, unless hot Baths relieve them."

Though in recent years a considerable amount of attention has been devoted by medical writers to the ætiology and treatment in children of a persistent inability to control bladder function, a similar disability in the aged has tended to be ignored by them, and in practice has almost invariably been regarded with a singular fatalism.

Sphincteric weakness resulting from senile muscular atrophy has persisted to be the common explanation of the condition advanced by most modern writers, but little or no evidence has been produced in support of this assumption. Langworthy et al. (1937), on the other hand, after studying aged incontinent patients, concluded that injury to the central nervous system was the most frequent cause of the disability, and Geist and Salmon (1943) relate the incontinence of some postmenopausal women to a senile vaginitis and œstrogen deficiency.

MECHANISM OF MICTURITION

The neurophysiology of the bladder and its sphincters has been described by so many workers that I do not propose to discuss in detail the mechanism of normal micturition. This has been admirably summarised by Denny-Brown and Robertson (1933) as follows:

> "The process of storage of urine and its evacuation occurs in a reservoir of which the distension excites a tendency to an automatic discharge.
>
> "The primary factor in discharge is contraction of the wall of the bladder with an accompanying secondary reciprocal relaxation of both sphincters.
>
> "Control of discharge and utilisation of the reservoir above about 50 c.cm. depends upon conscious and unconscious inhibition of vesical contraction. If necessary this may be reinforced by active voluntary excitation of the external sphincter until vesical contraction is overcome.
>
> "More usually the process pursues a course of progressive complete adaptation without the occurrence of sufficiently powerful vesical contractions to be accompanied by full relaxation of the internal sphincter until conscious or unconscious control of vesical contraction is released by voluntary effort."

The afferent and efferent arms of the reflex arc concerned in bladder contraction lie in the pelvic parasympathetic nerves, and the arc is completed in the 2nd, 3rd, and 4th sacral segments of the cord. Cortical control of the bladder, which is absent in the young infant but is normally acquired during the first few years of life, is exercised by means of inhibitory impulses transmitted from the cortex to the sacral region by spinal pathways situated in the dorsal halves of the lateral columns (McLellan 1939).

INCIDENCE OF URINARY DYSFUNCTION

Some degree of urinary dysfunction in the aged is so common that it has come to be regarded as almost normal. Of 35 male and 33 female chronic sick patients over the age of 70, only 5 and 9 respectively were free from urinary complaints. In both sexes the commonest symptom was increased frequency of micturition, and most of the patients also complained of precipitate, or imperative, micturition. The findings were as follows:

Sex	No. of patients	Difficulty	Slowness	Precipitancy	Frequency	Incontinence	No complaints
Male ..	35	3	7	19	22	11	5
Female ..	33	8	11	17	23	14	9
Totals ..	68	11	18	36	45	25	14

Many of the patients who complained of slowness or difficulty in initiating micturition related this symptom to nervousness or emotional upsets, and in several cases the information was volunteered that voiding was facilitated by hearing the sound of running water.

INVESTIGATION OF URINARY FUNCTION

For this investigation 36 aged males and females in the chronic sick wards were selected at random. Most of the patients investigated had some urinary dysfunction, 21 being incontinent, but some who did not complain of urinary symptoms were included in the series as controls. At the outset of the investigation, or shortly before it began, most of the 36 patients were bedridden, but most of them were mobilised, at least to the extent of being able to sit by their bedside, some being re-educated in walking-machines.

In each case the reaction of the bladder in response to gradual distension with fluid was determined with a simple cystometer (fig. 1). A 1 in 10,000 solution of potassium permanganate was warmed to about body temperature and allowed to enter the bladder at the rate of about 10 ml. a minute. Serial readings of bladder pressure recorded on the manometer were charted graphically against the volume of fluid instilled.

Technique

Before cystometric examination the patients were instructed to cough, and the presence of any stress incontinence was noted. They were then told to pass urine, after which they were placed on the couch, the females in the lithotomy position, and a catheter was passed with strict aseptic precautions, the residual urine being withdrawn and measured. The ease or otherwise with which a catheter was passed gave some indication of the degree of obstruction to the vesical outlet. At this stage the state of the vagina and urethral orifice could conveniently be observed, and the presence of cystocele, retocele, or senile vaginitis noted. In many cases a smear was made from the vaginal mucosa to determine the state of the epithelial cells.

The apparatus shown in fig. 1 was next connected to the catheter, the zero mark on the manometer having been

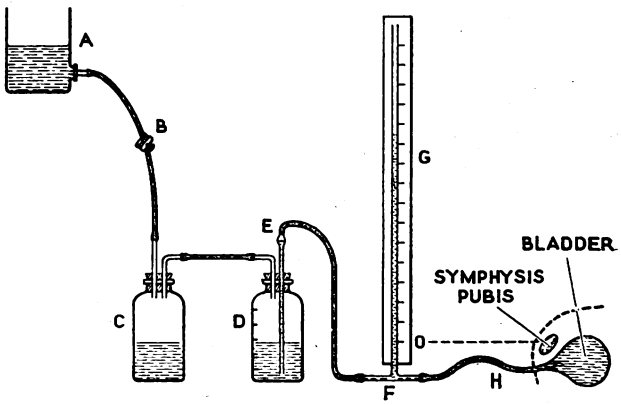


Fig. 1—Apparatus for cystometry: rate of flow from reservoir A into bottle C is controlled by screw-clip B; fluid entering bottle C displaces air, which in turn displaces potassium-permanganate solution from graduated bottle D past one-way valve E to T-junction F and thence via catheter H into urinary bladder. A rate of flow of 60 drops a minute into C gives a rate of flow of 10 ml. a minute into bladder.

Digitized by Google

adjusted to the same level as the symphysis pubis, and the pressure in the system being zero. The screw-clip B was adjusted so that fluid was entering the bladder at about 10 ml. a minute, and throughout the examination the screw-clip was regulated so that this rate of flow was kept constant. The one-way valve E ensured that during contractions the fluid was not forced back into bottle D.

During the examination the patient was questioned periodically about the presence of bladder sensations, and was instructed to hold his water, especially when a rise in pressure indicated a bladder contraction. That the patient was in reality attempting actively to inhibit bladder contractions could be determined by observing the voluntary musculature of the perineum for the presence of contraction, which is associated with such an inhibiting attempt.

The amount of solution instilled into the bladder did not exceed 400 ml. If, however, distension became painful before this amount was instilled, the instillation was discontinued. If no reflex bladder contraction had taken place during the period of filling, the patient was instructed to attempt to void before the apparatus was disconnected.

The apparatus was next disconnected from the catheter, and the bladder emptied. It is important that the bladder should be emptied, if possible, during an active vesical contraction, rather than passively drained through the catheter.

Besides cystometric examination, a standard clinical examination was carried out on each patient, with special reference to the presence of lesions of the central nervous system, urinary infections, senile vaginitis, prostatic enlargement, and local abnormalities of the bladder outlet. There were no facilities for cystoscopy and a more detailed knowledge of the state of the bladder than that afforded by routine methods was unobtainable. As already stated, any obstruction to the bladder outlet was indicated by difficulty in passing the catheter, though of course this is not an invariable criterion of obstruction. Patients with gross structural abnormality of the bladder or of its outlet were not included in the investigation. Of the 36 patients examined only 2 were thus excluded—a leaking suprapubic fistula being present in one case, and a complete procidentia in the other.

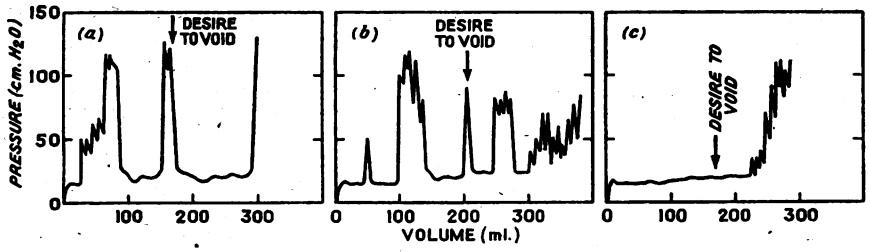


Fig. 2—Vesical pressure in a man, aged 71, who had increased frequency and precipitancy of micturition of several years' duration and was often incontinent: (a) at first cystometry; (b) a week later, showing improvement; (c) six weeks later, when symptoms had disappeared and patient said his urinary control was better than it had been for years.

RESULTS

On the entry of fluid into the bladder the pressure rose rapidly until the basic bladder tonus was reached. This reading varied from 8 to 18 cm. H_2O in different patients. Thereafter, unless bladder contractions took place, the curve of serial pressure readings ascended gradually until the instillation was discontinued.

In all the incontinent cases a point was reached at which the bladder did not accommodate further, and a sudden sharp rise in manometric pressure indicated contraction of the detrusor muscle. In spite of voluntary attempts to do so, the patients could not control the contractions, which were usually of considerable amplitude —as much as 125 cm. H_2O in some cases. These uninhibited contractions usually appeared early in filling, especially in the constantly incontinent cases, and almost invariably were not preceded by any sensation of desire to void. A typical vesical-pressure graph of such a case is shown in fig. 2*a*. Vigorous bladder contractions such as these, arising unheralded during physiological filling of the bladder, would undoubtedly lead to involuntary emptying of the viscus.

In the case of 3 constantly incontinent patients, however, in contrast with those already described, there was evidence of a moderate degree of adaptation of the bladder to distension, and contractions did not appear till comparatively late in filling. These patients were, however, completely confused and relatively inaccessible mentally, and it was evident in each case that the patient was not trying actively to control the bladder contraction. On the contrary, in 2 of the cases contraction of the abdominal musculature and relaxation of the perineum indicated a voluntary attempt to void. In these patients the incontinence was not a true dysfunction of the bladder mechanism, but rather a disorder of behaviour in which the patients voided urine (and often fæces) without reference to their surroundings, as the result of a dementia.

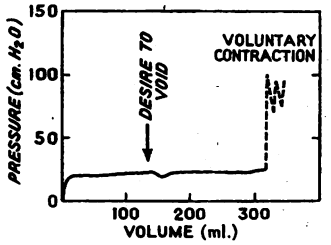


Fig. 3—Vesical pressure in a woman, aged 83, with no urinary complaint: bladder shows complete adaptation to instillation without uninhibited contractions.

Those patients in whom precipitate and overfrequent micturition was the main complaint, and in whom incontinence was only occasional, exhibited less bladder overactivity than did the constantly incontinent. Uninhibited contractions tended to arise later in filling, and there was occasionally prior, though admittedly short, warning of impending bladder contractions.

In patients who were free from urinary complaints the bladder either adapted completely during the instillation without contractions, or if contractions arose they were late in filling and were preceded at a considerable interval by increasing desire to void (fig. 3).

Most of the patients with precipitancy and incontinence noted an improvement in symptoms, occasionally dramatic, after cystometric examination. Frequency was less, and they had more control and could refrain from voiding for a longer time than before. In 10 of the 23 patients who complained of precipitancy or of incontinence the symptoms much improved or entirely cleared, and in 5 others some improvement was noted. Included in the 8 cases in which no improvement took place were the 3 patients whose incontinence was a disorder of behaviour rather than a dysfunction of the bladder mechanism.

Concurrently with the improvement in bladder function, cystometric evidence of increased bladder adaptation was observed. Uninhibited contractions arose later in filling than before and, where the incontinence had cleared, these contractions did not appear until an appreciable interval after the sensation of desire to void had been felt. Thus the patient had adequate warning of the state of bladder distension and could void voluntarily before the bladder was emptied reflexly (fig. 2).

The uninhibited contractions in some incontinent patients, more especially if the symptoms were long-standing, were poorly sustained and, though of normal amplitude, tended to subside rapidly. In these cases it was generally found that the bladder contained a consider-

Digitized by Google

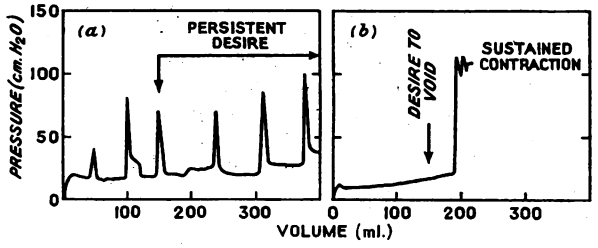


Fig. 4—Vesical pressure in a man aged 93: (a) while constantly incontinent, with residual urine 400 ml.; (b) a month later, when no longer incontinent, though micturition was still somewhat precipitate, and residual urine had decreased to 50 ml.

able quantity of residual urine. As bladder function improved with treatment, however, and overactivity was lessened, the contractions became more sustained and the quantity of residual urine decreased (fig. 4).

DISCUSSION OF RESULTS

The cause of incontinence of urine and, in a lesser degree, of precipitancy and urgency of micturition in the old people investigated was an overactivity of the reflex bladder mechanism in most cases.

A contributory factor to incontinence was, in some instances, a diminution of the visceral sensation of desire to void, with the result that the patient had little knowledge of the state of fullness of his bladder, or of the imminence of reflex voiding contractions.

In a few cases uncontrolled voiding resulted almost entirely from mental disorientation, and in only 3 cases did weakness or laxity of the vesical sphincter play an important part. In 2 of these patients there was a history of obstetric trauma, but the most patulous sphincter was detected in a nulliparous female with a hemiplegia.

Overactivity of the bladder mechanism resulted from a deterioration of the cortical inhibitory function, and from the presence of any local pathological state of the bladder of its outlet which tended to increase the excitability of the stretch receptors in the bladder wall. Of these two factors the former is the more important. In common with other cortical functions, it is not unreasonable to presume that inhibition of bladder activity participates in the general deterioration of efficiency which is a feature of senile involution within the nervous system. The actual cerebral lesion may be obscure. Neuronal atrophy, gliosis, and amorphous deposits have been described as occurring in the senile brain, and areas of softening, lacunæ of degeneration, small hæmorrhagic foci, and disseminated areas of atrophy often result from cerebral vascular disease (Critchley 1931). Commonly incontinence may be ushered in by a frank cerebral vascular lesion, often leading to hemiplegia.

Besides the deterioration of cortical inhibition resulting from structural damage to the nervous system there may also be a purely functional loss of inhibition. After a cerebral vascular lesion, injury to many of the nervous elements is transitory, and after a time recovery, or partial recovery, will ensue. Though the damage may not have been permanent, however, recovery of the function with which these elements were concerned may not take place until the patient has been re-educated in that particular function. Thus, as the recovering hemiparetic has to learn again the proper control of his limbs in walking, so, if the bladder inhibitory function has been in abeyance, control of bladder contractions must once again be acquired, as it was in infancy. Mitigating against the recovery of bladder control perhaps more than any other single factor is the semisomnolent state into which the aged patient so rapidly declines when confined to bed. In this vegetative existence the inhibitory function becomes involved in the general sluggishness of response to stimuli which is so apparent. In the present series the patients who were bedfast showed a much greater tendency to relapse after treatment.

Toxæmia and cerebral anoxæmia due to any cause, such as congestive heart-failure and severe anæmia, also tend to impair the inhibitory function, and thus lead to overactivity of the bladder.

Of the local pathological conditions a urinary infection is the most commonly detected. The incidence was high (50% of cases) and was relatively greater in females than in males. In some instances an acute urinary infection brought on precipitancy and incontinence, but in others chronic infections were found without any urinary dysfunction whatsoever. Infection was almost invariably present in the incontinent females, probably as a result rather than the cause, of the incontinence. Urination often improved in spite of the persistence of a chronic infection. A chronic urinary infection therefore does not appear greatly to increase the excitability of the bladder reflex. If the infection is acute, however, reflex excitability is much increased. Geist and Salmon (1943) have related the urinary incontinence of some postmenopausal women to a senile vaginitis and œstrogen deficiency causing impaired tonus of the vesical sphincter. Many of the female patients in this series had a senile vaginitis, which was in some cases improved by the administration of stilbœstrol. There was improvement in urination, with less reflex bladder excitability, after œstrogen therapy in these cases, but results were not dramatic, and no change was observed in the tone of the sphincters. It is considered, however, that a senile vaginitis helps to increase the excitability of the bladder reflex.

The incidence of enlarged prostate was no greater among the incontinent patients than among the continent. The rôle of prostatic enlargement in urinary dysfunctions is discussed below.

RATIONALE OF TREATMENT OF OVERACTIVE BLADDER

Maclachlan (1863), discussing the treatment of incontinence in the aged, stated:

> "Injections of cold water, perseveringly applied, the urine being first drawn off, are said to have been successful in numerous instances."

Braithwaite (1944) has noted dramatic relief following the graduated distension of the bladder with warm boracic solution in severe diurnal frequency in children which has not responded to ordinary measures. In the present series both subjective and cystometric improvement in bladder function resulted, in many cases, from the procedures comprising cystometric examination. The reasons for this are twofold, of which the first is considered the more important:

(1) During the filling of the bladder the patient is constantly urged to inhibit contractions. If a contraction takes place,

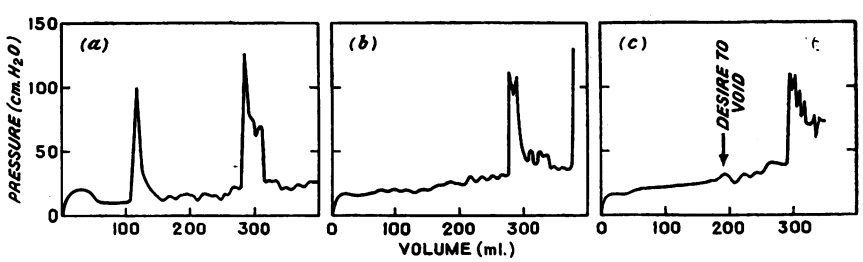


Fig. 5—Vesical pressure in a man, aged 76, with much enlarged prostate and 3 years' frequency, urgency, and incontinence, with residual urine 400 ml.: (a) at first cystometry; (b) a month later, when he had more control of micturition, though still occasionally incontinent, with residual urine 250 ml.; (c) two weeks later, when he had good control of micturition, with residual urine 80 ml.

Digitized by Google

there is no outlet for the fluid and the contraction registers as pressure on the manometer. Unless visceral sensation is much diminished, during such a contraction considerable discomfort is felt by the patient. This discomfort can be relieved only by inhibition of the contraction, and the patient is thus stimulated to inhibit strongly. In this way, if the inhibitory pathways are intact, the patient is re-educated in the inhibitory function.

(2) In some instances where the bladder has been emptying reflexly in response to the addition of small amounts of urine the fibres of the bladder wall have become shortened and the bladder has become small and contracted. In these cases gradual dilatation of the bladder with fluid will allow the muscles of the bladder wall to be stretched to an extent beyond the normal. This will decrease the sensitivity of the stretch receptors of the bladder wall, and may be regarded as a parallel to the full mobilisation of a limb which has developed a contracture. More usually, however, the uninhibited contractions of the incontinent patient only partially empty the bladder, and there is a gradual build-up of increments of residual urine. This build-up is assisted by the erroneous impression so often entertained by nurses that a patient who has just been incontinent does not require a bedpan or a bottle, and by the fact that the patient does not realise that his bladder has not been emptied. It is necessary to ensure that when voiding does take place it is as complete as possible. Such patients must be encouraged to empty their bladders voluntarily, even though they have only recently been incontinent.

Attempts should be made to eradicate any local condition which may cause bladder irritability. Finally, the patient should be stimulated to lead as active a mental and physical life as possible, and encouraged to try and control bladder function.

PROSTATIC ENLARGEMENT IN RELATION TO URINARY DYSFUNCTION

Enlargement of the prostate is closely linked with urinary dysfunction in elderly males, and the term "prostatism" is commonly applied to such a syndrome in these patients. In the present series cystoscopic examination of the prostate was impossible, but some degree of obstruction was detected in as many patients without precipitancy or incontinence as it was in patients with these complaints. Where frequency and precipitancy of micturition were accompanied by enlargement of the prostate, these symptoms improved in most cases after cystometry, and the efficiency of the urinary mechanism increased, with reduction of residual urine (fig. 5).

In progressive enlargement of the prostate two factors come into play: (1) increasing obstruction to the vesical outlet; and (2) an increase in the irritability of the bladder. As a result of the obstruction, difficulty in initiating micturition and possibly dysuria arise, and later, if the obstruction increases, retention of urine develops. In response to the increasing obstruction, the bladder wall becomes hypertrophied and trabeculate. Increase in bladder irritability, if the cerebral inhibitory function is not impaired, gives rise to increasing frequency of desire to micturate. If, however, there is diminished cerebral control, as is so often the case in such patients, the increased bladder irritability is sufficient to cause the bladder reflex to break through the diminished cortical control, giving rise to uninhibited bladder contractions and urgent and precipitate micturition, perhaps with incontinence. As a result of the overactivity the bladder contractions are less efficient, and the amount of residual urine is increased. Thus the balance between the degree of obstruction to the vesical outlet and the efficiency of the neuromuscular mechanism of the bladder is of prime importance. In the presence of minimal prostatic obstruction large quantities of residual urine may be found as a result of inefficient bladder contractions (fig. 4).

Clarke (1937) has described cases of prostatic syndrome in which the symptoms disappeared spontaneously after cystoscopy. The amelioration of symptoms in many of these cases may have been due to improvement in vesical function following the instillation of fluid similar to that occasioned by cystometry.

In the investigation of cases of prostatic obstruction, therefore, it is considered that, besides estimating the degree of obstruction to the bladder outlet, the functional efficiency of the neuromuscular mechanism of the bladder must be assessed by cystometry, and if possible the function improved.

SUMMARY

The common urinary dysfunctions in the aged are increased frequency and precipitancy of micturition, often accompanied by incontinence.

The cause of these symptoms is mainly overactivity of the neuromuscular mechanism of the bladder. Sphincteric weakness is important in only a small minority of cases.

Overactivity of the bladder mechanism results from diminution of cortical control and from local irritative conditions of the bladder and its outlet. These factors operate to different extents in different cases but commonly the former plays the more active rôle.

Impaired cortical control may be due to structural changes within the nervous system and to a functional loss of inhibitory power. An impaired mental state is a contributory factor, as also is the confinement of the elderly patient to bed.

In many cases of overactivity of the reflex bladder mechanism function improves as a result of gradual distension of the bladder with fluid and inhibitory re-educative training.

The efficiency of the neuromuscular mechanism of the bladder is doubly important in prostatic enlargement. The routine investigation of the prostatic syndrome in the aged should include cystometry, so that the bladder function may be assessed and, if possible, improved.

REFERENCES

Allen, J. (1733) Practice of Physick. London.
Braithwaite, J. V. (1944) *Post-grad. med. J.* **229**, 350.
Clarke, R. (1937) *Brit. J. Urol.* **9**, 254.
Critchley, M. (1931) *Lancet*, i, 1119, 1221, 1331.
Denny-Brown, D., Robertson, E. G. (1933) *Brain*, **56**, 149.
Geist, S. H., Salmon, U. J. (1943) *J. Mt Sinai Hosp.* **10**, 208.
Langworthy, O. R., Jarvis, J. A., Lewis, L. G. (1937) *Sth. med. J.* **30**, 969.
Maclachlan, D. (1863) A Practical Treatise on the Diseases and Infirmities of Advanced Life. London.
McLellan, F. C. (1939) The Neurogenic Bladder. Springfield.

". . . Few would deny the advantage of good build, fast and accurate neuromuscular coördination, strength, physical health and a high natural resistance to disease. We can surely encourage those endowed with such qualities to regard themselves as proper parents for the next generation. But in the field of temperament, our aims are much less clear. There is no such thing as a good and desirable type of temperament, and a bad and undesirable one. It takes all sorts to make a world. There is room for the quiet, the docile and the stable; but there is room also for the man of strong passions, for the natural born rebel, for the man whose moods take him from phases of elation and enhanced activity into troughs of depression. It is true, indeed, that a man like Hitler can cause much greater harm to humanity than even a million mental defectives; but we cannot say, if Hitler had had children, that they would have been any more likely to have been bad citizens than anyone else's. It is particular combinations of temperamental qualities which are productive of large effects, good or bad. Recombined in another way, the effect of the genes responsible would have been different. In fact we are too uncertain of where we want to go, and too ignorant of the foundations on which we stand, for there to be at present a practical eugenic approach to the betterment of human personality."
—Dr. J. A. FRASER ROBERTS and Dr. ELIOT SLATER, *Eugenics Review*, July, 1948.

Digitized by Google

SPONTANEOUS RUPTURE OF THE RECTUM

REPORT OF A CASE

CHARLES P. ALLEN
M.B. Lpool, F.R.C.S.E.
LATE RESIDENT SURGICAL OFFICER, KING GEORGE HOSPITAL, ILFORD

TRAUMATIC rupture of the rectum appears to be fairly common, but not spontaneous rupture.

Lindenbaum [1] collected the records of 26 cases, including one reported in 1827 by Brodie, who apparently was the first to describe this condition. Of these 26 patients 24 died. In 23 cases rupture was associated with effort: 12 during defæcation, 4 during weight-lifting, and the remainder after a fall, while vomiting, during micturition, during childbirth, or during the return of the prolapsed rectum after purgation. In 13 cases rupture was associated with prolapse of the rectum, and in 2 with cancer. In 8 cases no pathological abnormality was found. Guibé [2] describes 1 case in which the rectum was ruptured during sleep.

The following case appears to be one of the rare spontaneous ruptures not associated with strain or any pathologic abnormality.

A male photographic process operator, aged 54, felt a sudden moderately severe pain in the lower part of his abdomen while walking to work after his midday meal.

The pain, at first felt chiefly in the hypogastrium, gradually spread over the whole abdomen, but he continued with his work until 4.15 P.M., when he was obliged to return home because of the severity of the pain. In response to a "feeling of fullness in the back passage" and a sensation that "something wanted to come away" he took a dose of Glauber's salt, which he immediately vomited.

He reached hospital via his doctor just before midnight and gave a history of many years' chronic constipation, but had for about six weeks not found it necessary to take purgatives. There was no history of passing blood or mucus; his bowels were opened naturally early that morning, and enemas were never used.

Examination revealed generalised abdominal rigidity and absence of abdominal breathing, with tenderness more acute in the right inguinal fossa and in the right epigastrium. Liver dullness and bowel sounds were absent. Rectal palpation revealed a walnut-sized swelling in the pouch of Douglas, with tenderness more acute on the left side. Anus of good tone and not patulous. Slight cough, and a few râles at both lung bases. Blood-pressure 160/80. Temperature 101·6°F, respiration 22 per min., pulse-rate 78.

Laparotomy.—About eleven hours after onset of symptoms his abdomen was opened through a right paramedian infra-umbilical incision. Peritoneal cavity contained purulent fluid. Appendix normal.

A mass of fæces about 1 in. in diameter and of the consistence of fresh putty was lying free in the pelvis, and a transverse tear $1^1/_2$ in. long was found in the anterior wall of the first part of the rectum.

The slit in the mucosa was not indurated or friable, and there was no hæmorrhage. Rectum and pelvic colon otherwise normal. No evidence of foreign body. Small intestine had not prolapsed through tear.

Tear was sutured in two layers, and a suprapubic pelvic drain inserted. Operation completed by left inguinal colostomy.

Progress.—Postoperative treatment included sulphadiazine and penicillin. Patient made an uninterrupted recovery. Three months later colostomy was closed by intraperitoneal method.

I wish to thank Mr. Neil Sinclair, senior surgeon to King George Hospital, Ilford, for permission to publish this case.

1. Lindenbaum, I. S. *Arch. klin. Chir.* 1936, **187**, 478.
2. Guibé, M. *J. Chir., Paris*, 1931, **37**, 645.

CONGENITAL TORTICOLLIS IN IDENTICAL TWINS

A. E. STEVENS
M.B. Lond., F.R.C.S.E., D.T.M. & H.
ASSISTANT SURGEON, REDHILL COUNTY HOSPITAL, SURREY

THERE are many records of the same abnormality in identical twins, but none of torticollis.

The following two cases of torticollis were in identical twins born on July 5, 1935. Unfortunately no details of their obstetric history can be obtained, since they were born in a nursing-home which has since been closed, and their mother died three months after their birth. Their aunt, who looks after them, does not know of any abnormality during labour. There is no history of torticollis or of hereditary disease in any other member of the family; and, apart from the fact that one child had strabismus, they had no other congenital abnormalities. The twins are otherwise healthy and normal.

They were admitted to the Redhill County Hospital on March 10, 1947, with an identical well-marked right torticollis. In both cases the clavicular head of the sternomastoid muscle was more contracted than the sternal head, and there was a small bony swelling at the insertion of the muscle into the clavicle. There was no sternomastoid "tumour." There was obvious right facial hemiatrophy and an early scoliosis of the upper dorsal and lower cervical spine. The physical defect was the same in the two cases.

As both twins had an eye defect, the question of ocular torticollis was considered, though they did not show all the features of this disease. They were therefore referred to Mr. G. J. Ahern, county ophthalmologist, who reported as follows:

"Twin no. 1 had a left convergent concomitant squint of 15°. There was no suggestion of a vertical deviation which goes with an ocular torticollis. I consider she has a straightforward left convergent concomitant squint due to difference in the refraction of the two eyes, and that her torticollis is incidental.

"There is no evidence of strabismus in twin no. 2. Her visual acuity is subnormal. There is nothing very strikingly similar in their eye defect. Lastly, the only similarity is in twin no. 1's left eye and twin no. 2's right; and, if this was playing any part in their torticollis, one would expect the head tilt on opposite sides."

At operation on March 11, the sternomastoid muscle and deep fascia were divided, after which the twins made a satisfactory recovery. When they were last seen, on Aug. 18, neck movements were normal.

Many causes of congenital torticollis have been suggested, including heredity, ischæmia, and trauma. Mercer [1] states that trauma is generally held to be the primary cause. McMurray [2] gives the theory that the contracture of the sternomastoid is similar to that occurring in Volkmann's ischæmic contracture and is due to thrombosis of the end-artery which supplies the middle part of the sternomastoid muscle. There is no record of a sternomastoid swelling in these twins, and it must be assumed that the torticollis is congenital. Illingworth and Dick [3] consider that there is no single cause of congenital torticollis; that some cases must be attributed to developmental aplasia of the affected cervical segments; and that this is the usual cause. In these twins a traumatic origin can be virtually excluded, for it is most unlikely that they suffered precisely similar trauma. A congenital developmental error is the probable explanation.

I have to thank Mr. Norman Pitt, medical superintendent of Redhill County Hospital, for his interest and encouragement; and Mr. Ahern for his report on the eye condition.

1. Mercer, W. Orthopædic Surgery. London, 1945.
2. McMurray, T. P. A Practice of Orthopædic Surgery. London, 1943.
3. Illingworth, C. F. W., Dick, B. M. Textbook of Surgical Pathology. London, 1945.

Digitized by Google

Preliminary Communication

EXSANGUINO-TRANSFUSION IN ACUTE LEUKÆMIA

IT is, of course, still true that no method of treatment will cure acute leukæmia, but that is no reason for complete inactivity on the part of the physician, because in many—perhaps most—cases, it is possible to induce a remission. Since nothing is known of the cause of leukæmia in man, treatment must necessarily be empirical; nevertheless, one's views on the cause of the disease may influence the choice of treatment. Those who hold that the leukæmic process is neoplastic will tend to favour radiotherapy, though in acute leukæmia it is worse than useless. If, on the analogy of avian leucoses, the disease is regarded as infective, the temptation is to try the various antibiotics. But holders of either of these theories are, not unnaturally, inclined to therapeutic nihilism, because there is no effective treatment for generalised malignant tumours or for the virus diseases.

On the whole, the consensus is in favour of the neoplastic theory, perhaps mainly because the cellular characters are reminiscent of those characteristic of malignancy. That is true enough, but similar cytological appearances are found in the immature red cells in pernicious anæmia, which is not neoplastic, though about 30 years ago there was a tendency among pathologists to think that it was.

Few, if any, writers have suggested that the cellular changes are secondary to abnormalities of the milieu interne—in other words, that the dedifferentiation or undifferentiation of the leukæmic cells follows changes in the blood-plasma. That this is a possibility is suggested by the observation of Schwind,[1] that injection of normal blood-plasma leads to diminution in the number of myeloblasts in the blood, which seems to indicate that the pathological process in the hæmopoietic tissues is not entirely autonomous. Then again, Israëls[2] found that, in tissue culture, leukæmic myeloblasts could mature into myelocytes—a clear indication that they are not totally disordered, but that their abnormalities depend on their environment. Another significant point is that Dreyfus,[3] after a careful and extensive study of the literature of remissions in acute leukæmia, has shown that there is a direct relation between the likelihood of a remission and the number of blood-transfusions and the total amount of blood infused.

Then came the remarkable reports of Bessis and Bernard,[4] who performed a replacement transfusion in a case of acute leukæmia and produced an immediate remission. Occasional injections of 100 ml. of blood, together with penicillin whenever sepsis occurred, prolonged the remission for months. I had the opportunity of seeing such a case in Paris. A man of 40 developed a remission of acute leukæmia after an exsanguino-transfusion and nine months later is still in fair health, though it has been necessary to give about 100 ml. of blood every fortnight and also short courses of urethane when the leucocytes rise unduly high. As Bessis will publish details of this case I cannot give more information about it, but I wish to call attention to some of the remarkable changes that followed replacement transfusion in the following case of acute leukæmia.

A woman, aged 34, had been diagnosed as suffering from acute leukæmia about two months before I saw her, and had been given about 4 pints of blood. Then, because it is impossible to obtain very large quantities of blood at any one time in England (a matter I hope to discuss in another article), the patient was taken to Paris, where Tzanck performed exsanguino-transfusion in two parts, with an interval of two days between.

The hæmogram, when the patient left London, was:

Red cells	2,600,000 per c.mm.
Hæmoglobin	45%
Leucocytes	96,000 per c.mm.
Platelets	very scanty indeed.
Polymorphs	12%
Lymphocytes	1%
"Blasts" of monocytoid type	87%

The day after she had been transfused with 7 litres of blood, while 6½ litres was withdrawn, her hæmogram was:

Red cells	4,500,000 per c.mm.
Hæmoglobin	90%
Leucocytes	18,400 per c.mm.
Platelets	236,000 per c.mm.
Polymorphs	18%
Eosinophils	2%
Basophils	1%
Metamyelocytes	14%
Myelocytes	5%
"Blasts"	58%
Lymphocytes	2%

Twenty-four hours after a further 7 litres had been infused and the same amount withdrawn, the hæmogram was much the same, except that the leucocytes had fallen to 12,000 per c.mm., while the red cells showed a good deal of anisocytosis and polychromasia. Five days later the blood picture was practically unchanged; and the patient, who had been extremely ill, was feeling well; she was afebrile and had lost the exquisite tenderness of the sternum that had been very striking when I first saw her. The spleen, which had been palpable (about two fingers), was unchanged.

There is, of course, no way of determining how long the remission will persist in this case, but one can hope that, using Bessis's technique (frequent "topping up" with small blood-transfusions, and urethane) it may be possible to prolong it, perhaps until the disease passes into the chronic form.

The aspect of the matter that seems to me to be of such great importance is that such exsanguino-transfusions bring about a distinct change in the cellular composition of the blood and hæmopoietic organs, which is not simply attributable to the blood that has been infused but is a vital reaction on the part of the patient. Whether, in the leukæmias, the plasma is deficient in some substance required for the maturation of white cells, or whether it contains some substance that stimulates them to divide so rapidly that maturation is impossible, I do not know. But that there is here a possibly fruitful line of research seems to be obvious.

Two striking points have already emerged. First, it is notorious that massive transfusions are badly tolerated in acute leukæmia, whereas exsanguino-transfusions cause only a minimal upset: urticaria and a few small rigors are not uncommon after about 5–6 pints has been drawn off and the same amount infused. Secondly, the published cases show that the remissions are not purely symptomatic, for both blood and marrow revert to a much more normal composition; and the remission is progressive, improvement occurring steadily for days or weeks—it is not a case of living on borrowed blood.

It is much too early to theorise about the mode of action of exsanguino-transfusion, but of its value there can be no doubt. One patient so treated has lived in good health for over 20 months (to be published by R. Cattan). To the hæmatologist, one of the most remarkable facts is that a relapse may be heralded by a sudden neutrophilia, and not, as one would have expected, by an increase of "blasts."

A. PINEY
M.D. Birm., M.R.C.P.
Physician.

St. Mary's Hospital for Women and Children, London.

1. Schwind, J. L. *Amer. J. med. Sci.* 1947, **213**, 170.
2. Israëls, M. C. G. *J. Path. Bact.* 1940, **51**, 235.
3. Dreyfus, R. *Le Sang*, 1948, **19**, 35.
4. Bessis, M., Bernard, J. *Bull. Soc. méd. Hôp. Paris*, 1947, p. 871; *Le Sang*, 1948, **19**, 45.

Digitized by Google

Reviews of Books

Oral and Dental Diseases

HUBERT H. STONES, M.D., M.D.S., F.D.S. R.C.S., professor of dental surgery and director of dental education, University of Liverpool. Edinburgh: E. & S. Livingstone. 1948. Pp. 896. 90*s*.

THIS is an excellent book. It is clear, concise, and well illustrated, and has full references at the ends of the chapters, so that anyone wishing to obtain further information can do so with the minimum of trouble. It deals mainly with the pathology of oral and dental diseases with clinical signs and symptoms. In some sections indications for operative as well as conservative treatment are given. In a work such as this the descriptions of operative treatment are necessarily brief: and, for example, the illustrations showing methods of removal of the mandibular third molar, though good in themselves, might perhaps have been omitted. But it is a pleasure to read a book in which one finds so much up-to-date information so clearly imparted.

Vascular Diseases in Clinical Practice

IRVING SHERWOOD WRIGHT, M.D., associate professor of clinical medicine, Cornell University. Chicago: The Year Book Publishers. London: H. K. Lewis. 1948. Pp. 514. 42*s*.

THIS "general practice manual" covers the whole subject from methods of examination, through clinical features, to treatment, and concludes with a valuable chapter on the industrial and medicolegal aspects of peripheral vascular disease. That it is up to date is clear from the inclusion of references to tetraethylammonium salts and rutin. Anticoagulant therapy is also fully discussed, with emphasis on the value of dicoumarol as opposed to heparin. We doubt whether a book such as this should contain a special chapter on "hypertensive ischæmic ulcers of the leg," and in the chapter on varicose veins more attention might have been paid to types of bandage. But, all in all, this is a reliable introduction to a difficult subject of increasing importance.

Pain

HAROLD G. WOLFF, M.D., associate professor of medicine, Cornell University Medical School, New York; STEWART WOLF, M.D., assistant professor of medicine in the school. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 86. 10*s*. 6*d*.

Spasticity

The Stretch-reflex and Extrapyramidal Systems. H. W. MAGOUN, PH.D., professor of microscopic anatomy, Northwestern University medical school, Chicago; RUTH RHINES, PH.D., instructor in anatomy in the school. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1947. Pp. 59. 10*s*. 6*d*.

THESE two volumes are designed to present to the non-specialist reader the results of recent neurophysiological research and its significance for clinical problems.

The book on pain begins with an account of psychophysiological investigations upon the threshold for pain and its measurement. The "bright" and "burning" elements in cutaneous pain are distinguished and discussed, and deep pain and its reference are analysed. After this the anatomy and physiology of painful states of the various organs of the body are considered, the section on headache being particularly good, as might be expected seeing how much Prof. H. G. Wolff has contributed to its elucidation. In conclusion there are brief sections on the medical and surgical control of pain. As must happen in a small book dealing with a large subject the treatment of some topics is rather sketchy, and Thomas Lewis is only mentioned obliquely as the source of an erroneous belief. Nevertheless this is a useful and stimulating account of some aspects of the neurophysiology of pain.

Professor Magoun and Dr. Rhines regard spasticity as an exaggeration of the stretch-reflex. They accept the view of Fulton and his collaborators that it is not caused by damage to the pyramidal tract, and they attribute it mainly to interruption of reticulospinal pathways which normally exert an inhibitory influence on it and which are themselves influenced by the cerebellum, the striatum, and the suppressor area of the cortex (4 S). This is a good review of one aspect of the subject, but the authors' uncritical acceptance of the ideas of the Fulton school has led them to take an over-simplified view, which, as they recognise, leaves unsolved the problem of the spinal paths concerned. The book is almost entirely neurophysiological, and in order to explain spasticity in man the neurophysiologist must have the help of the clinician.

Biology of Pathogenic Fungi

Editor: WALTER J. NICKERSON, PH.D., lecturer in medical mycology and dermatology, Tufts College. Waltham, Mass.: Chronica Botanica Co. London: Wm. Dawson and Sons. 1947. Pp. 236. 30*s*.

THE editor of this volume has collected essays by experts from various countries, covering aspects of medical mycology in which advances have recently been made.

J. Lodder (Delft) and A. de Minjer (Utrecht) discuss torulosis (blastomycosis of the central nervous system) and conclude that only a single species of yeast is involved. A. L. Carrión and Margarita Silva (San Juan, Puerto Rico) give an account of the several fungi causing chromoblastomycosis. Rhoda W. Benham (New York) describes the isolation and nutrition of *Pityrosporum ovale*, the yeast universally present in dandruff scales, which is unusual among micro-organisms in requiring fatty substances for growth. C. W. Emmons (Bethesda, Maryland) summarises recent progress in the study of coccidiodomycosis, a disease with an animal reservoir in wild rodents in the Arizona and California deserts. R. Ciferri and P. Redaelli (Pavia) describe recent work of the Italian school of mycopathology. Frederick T. Wolf (Nashville, Tennessee) writes on the action of sulphonamides and antibiotics on pathogenic fungi. The geographical distribution of systemic fungus diseases is reviewed by D. S. Martin of Durham, North Carolina. The volume concludes with four chapters on the biochemistry of fungi contributed by the editor, by R. L. Peck (Merck Laboratories), and by J. W. Williams (Bay Pines, Florida).

The work is intended rather for the laboratory worker and specialist than for the clinician. Although necessarily covering only part of the field, it is a welcome contribution to the study of the pathogenic fungi as living organisms.

A Manual of Removable Partial Denture Design (Toronto: University of Toronto Press. London: Oxford University Press. 1948. Pp. 99. 20*s*.).—This is a purely technical book, showing illustrations and types of partial dentures, by the professor of prosthodontia at Toronto, Mr. R. J. Godfrey. Dental surgeons will find it very useful.

New Inventions

A MATCHED SET OF NEEDLE-HOLDERS

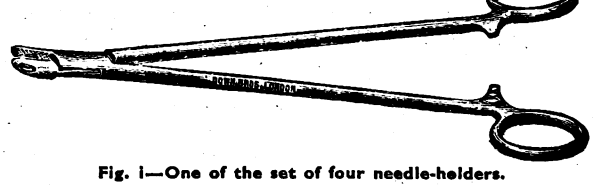


Fig. 1—One of the set of four needle-holders.

THE needle-holder illustrated here (fig. 1) has been designed to have a dependable grip (fig. 2) which lends itself to the tying of "no-touch" knots, a light spring in the shafts to prevent the hand becoming tired, and rings well-rounded for comfort and a little larger than usual, to admit the occasional thickened fingers of the older surgeon.

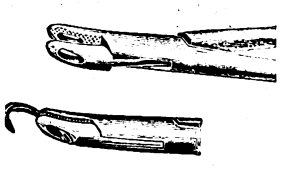


Fig. 2—Tip of needle-holder giving specially reliable grip.

The needle-holders are made in sets of four lengths—5 in., 6 in., 7 in., and 8 in.—to allow for various depths of wounds. Messrs. Down Bros. are the makers.

London. HAROLD DODD, F.R.C.S.

Digitized by Google

PRESSURE DRESSING FOR A SCALD

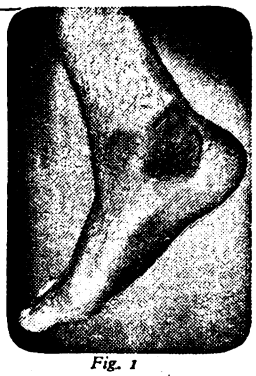


Fig. 1

AUGUST 22nd, 1947. Scalded at work. Next day attended hospital with a large blister of inner aspect R. ankle (Fig. 1)

Treatment. Scalded area dressed with Jelonet (tulle gras), Viscopaste bandage applied from toes to knee. Pressure pad of cotton-wool applied over scalded area. The whole leg firmly bandaged with Elastocrepe, with especially firm pressure over the scalded area. (Fig. 2).

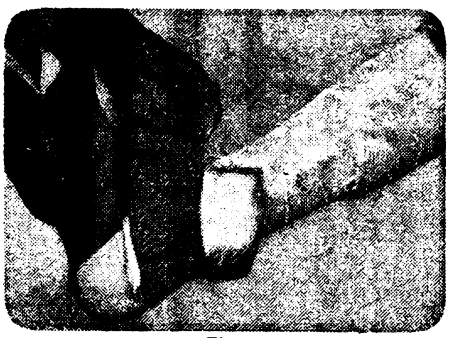


Fig. 2

7th October, 1947. When bandages were removed, wound soundly healed. (Fig. 3).

Comment. Firm pressure dressing afforded *immediate* comfort, permitting ambulatory treatment and continuation at work.

These details and illustrations are of an actual case. T. J. Smith & Nephew, Ltd., of Hull, manufacturers of Elastoplast, Elastocrepe, Jelonet and Viscopaste, publish this instance—typical of many—in which their products have been used with success.

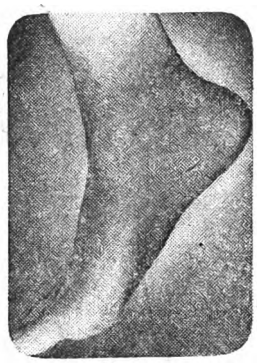
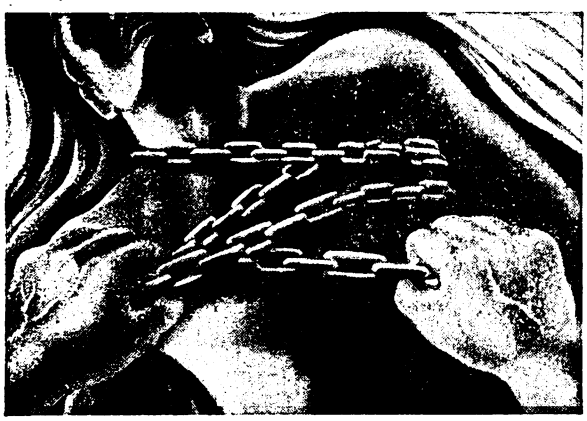


Fig. 3



for
Bronchial Asthma

"A SAVORY & MOORE PRODUCT"

NEODRENAL
BRAND
ISOPROPYL ADRENALINE
THE NEW "ORAL" ADRENALINE

WELL TOLERATED · LITTLE EFFECT ON BLOOD PRESSURE

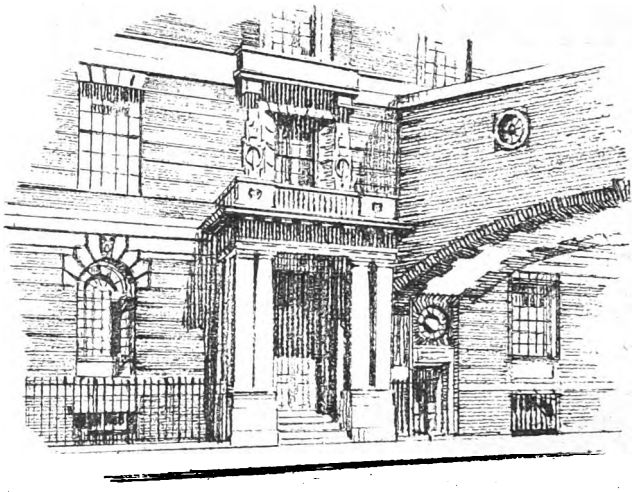
Issued in the form of tablets for sublingual use and a spray solution for oral inhalation.

Literature and Samples on request :—

SAVORY & MOORE LTD, WELBECK STREET, LONDON, W.1

Digitized by Google

St Mary's Hospital



Entrance to the Wright-Fleming Institute of Microbiology, St. Mary's Hospital, London.

VACCINES

for respiratory affections

Anti-Catarrh Vaccine

The ideal time for commencing prophylaxis against the common "cold" is during September. Three graduated doses, or six if preferred, with an interval of from 7 to 10 days between each, are recommended. The vaccine especially designed for the purpose is "Anti-Catarrh Vaccine," containing *M. Catarrhalis*, with *Pneumococcus, B. Pneumoniæ, B. Septus, B. Influenzæ*, and *Streptococcus. This vaccine is supplied in sets of 3 or 6 graduated doses, and in ampoules of 1 c.c.; also in bottles of 10 c.c. and 25 c.c.*

Influenza Virus Vaccine

A purified and concentrated vaccine for protection against both types A and B influenza virus. It is recommended that a first dose of 1 c.c. be administered in September, or early in October, followed by the same dose after two or three months. To afford protection against the secondary as well as against the primary infection, Influenza Virus Vaccine may be combined with Anti-Influenza Vaccine (Mixed).

Supplied in 1 c.c. ampoules

These vaccines are prepared in the Wright-Fleming Institute of Microbiology (late Inoculation Dept.), St. Mary's Hospital, London, W.2. Further particulars on request.

Sole agents:

PARKE, DAVIS & CO., HOUNSLOW, MIDDLESEX

Inc. U.S.A., Liability Ltd.

Digitized by Google

THE LANCET

LONDON: SATURDAY, SEPT. 4, 1948

Food and Peoples

"IF we cannot solve the problem of world resources in this century, we are heading for the greatest catastrophe in history." Sir JOHN ORR'S blunt warning, at the Congress on Population and World Resources in Relation to the Family, held at Cheltenham last week and reported on p. 388, was delivered to apt hearers. The congress was arranged by the Family Planning Association of Great Britain, and attended by delegates from an extremely wide range of countries. Discussion throughout four days centred round the twin problems of a growing world population and the difficulties which must be faced if they are to be fed. The situation can be approached in two ways—either we must plan to increase food production enormously and to solve the outstanding puzzles of distribution; or we must find ways to stabilise populations. Probably we shall only just avoid disaster if we use both methods intelligently and with all our might. Sir JOHN ORR and his colleagues on the Food and Agriculture Organisation inevitably concentrate on the first, while family planners look with confidence to the second as a long-term policy offering some hope of world salvation.

The possibilities of greater food production are decidedly promising if they can be put into effect. By better methods of agriculture and better plant selection, by cultivating more ground, and by reclaiming ground now being destroyed by soil erosion, the yield can be much augmented. All this will be wasted effort, however, if distribution is not made more equitable. To produce *enough* food is merely a piece of virtuosity if a few nations are to eat well above subsistence level while others live far below it. For a time at least we may have to be content with a simpler diet—on the lines, perhaps of Mr. ROY WALKER'S diet of brown bread, milk, and vegetables—if we are all to eat at all. Other experiments are beginning to promise results: the cultivation of plants in water to which the necessary chemicals have been added, and the chemical synthesis of foodstuffs were mentioned at the congress. None can say how far such methods can be developed, or how men a few centuries hence will be feeding themselves. But unless some unforeseen and revolutionary changes take place we must double our food production within the next 25 years if we are to feed the 3000 million people who will be alive at the end of the century: otherwise the hungry generations will tread us (and each other) down in quite a new sense from that which troubled KEATS. As Sir JOHN ORR pointed out, hungry people do not die quietly; and why should they?

The food issue, however, is fairly straightforward, while that of population is tortuous. Dr. C. P. BLACKER'S five stages in the demographic cycle seem to promise an ultimate stability, or even decline, in the world population; but the trouble is that national populations are at different stages in the cycle. Thus France has already passed the fourth stage (in which there is a low birth-rate and death-rate, and a stationary level of reproduction) and is passing into the fifth stage of decline. Great Britain and the United States are likely to follow suit. The U.S.S.R. is in the third stage, in which the birth-rate is falling but the death-rate falling faster; while large parts of Asia and Africa are in the first stage (with a high death-rate and a high birth-rate), or the second stage (with a high birth-rate and a falling death-rate). The danger is that if population growth is left to develop on its own lines the hungry, fertile, and overcrowded nations will in the end be driven to go to war with those which are stable and well fed. Migration, it seems, is no solution. In the long run it will be to the advantage of nations in the later demographic stages to help the rest to eat and live better, for it is a constant demographic observation that the birth-rate falls when standards of living rise. Nor is this the fate of man alone: animals and insects are similarly affected. Thus populations of butterflies living under adverse conditions are commonly very fertile; whereas they reproduce much less freely when conditions improve. It is as though when conditions are bad nature ensures race survival by providing a surplus; when conditions are good she can afford to be more parsimonious. Certainly birth-control alone is not responsible for the population change which follows in the train of better standards of living. What other factors come into play are a matter of speculation, and were not discussed at the congress. One may be the later marriage common in communities where young people find it worth while to work and save in order to launch themselves more comfortably. Another may be, as Mr. F. M. MANSOUR suggested, that a large family is a constant source of occupation and pleasure to those who have few other interests; whereas in a community offering a wider range of interests, especially to women, the family no longer holds undisputed place. Again, it is not often possible in the crowded homes of an industrial town to raise a large family: some means of restriction has to be found. None of these arguments, however, applies to butterflies—or indeed to any other animal than man—and there may well be biological factors at work on the germ plasm of which we know nothing. How much effect contraceptives have on the size of populations is hard to determine; possibly their main value is to the individual. Spacing of children benefits both mother and children, protecting the lives and health of both; and it is noteworthy that in the United States, as Dr. ABRAHAM STONE pointed out, all Churches agree that such planning adds to the stability of the family, though some Churches consider observance of the "safe" period to be the only justifiable contraceptive measure.

Whether the dissemination of contraceptive technique in countries now in the first two demographic stages would help to stabilise populations and prevent "swarming" requires close and quick study. At all events it is worth trying. Unfortunately it presents special technical problems, since most of these countries are in tropical or subtropical latitudes. Most contraceptive appliances are of rubber, which perishes easily in heat, and most chemical contraceptives are made up in bases designed to melt at body temperature. It seems likely, from the reports of speakers at

Digitized by Google

the congress, that the women in these countries would welcome advice on the spacing of children; and there is little danger that the spread of such advice would lead to race suicide since fertility is very highly valued in such countries. Yet until an appropriate and accessible contraceptive can be devised for hot climates, such advice cannot be an effective measure for population control. In the task of solving this and other problems of fertility the new international committee for research into family planning, set up at the congress, will have an important part to play. In the long run, however, the best means of reducing the birth-rate may be to raise world standards of living—a policy worth achieving on many grounds. We are constantly getting opportunities to look ahead and plan our destiny, though we generally ignore them. This seems to be a situation in which duty and interest point the same way—towards an effective world plan for food and a rise in living standards. As the Rev. JOSEPH MCCULLOCH put it, man is born to know more and more what he is doing. His survival may well depend on his ability to accept this privilege and responsibility.

Function and Dysfunction of the Bladder

THE normal function of the bladder has received too little attention from the clinician. This viscus is unique in that, though its activity depends on an autonomic reflex, during life a considerable degree of voluntary control is acquired. Perhaps for this reason, the factors affecting bladder function are many and varied—and as yet imperfectly understood. The mechanism of micturition has been clarified to a considerable extent by the physiologists. It is generally agreed that the activity of the bladder depends on a reflex arc, both arms of which lie in the pelvic parasympathetic nerves, and which is completed in the 2nd, 3rd, and 4th sacral segments of the cord. The exciting stimulus is provided by distension of the bladder. In addition, an overriding cortical control of bladder activity is exercised by inhibitory impulses relayed from the higher centres to the sacral region by spinal pathways. The site of impact of these impulses is thought by DENNY-BROWN and ROBERTSON [1] to be on outgoing neurones of the spinal cord, and they in some way interfere with the completion of the reflex arc. Thus a person may have a sensation of bladder distension, but the viscus will not normally contract until inhibition is voluntarily removed. Desire to void urine depends on bladder distension and also on the rate of distension; the more rapidly the bladder is filled the earlier the desire appears. But a strong and urgent desire to void also arises during bladder contractions: hence the micturition accompanying bowel opening and hence the desire to void brought on by the psychical stimulus of hearing running water. Intravesical pressure, which is the sum of the pressure exerted by the tonicity of the bladder wall and the intra-abdominal pressure, may vary independently of bladder-distension. Thus in laughing the intravesical pressure rises but the distension remains the same, and desire to void will not be brought on unless the intravesical pressure was already so high, or the urethral sphincter so weak, that the internal sphincter is forced and the series of bladder reflexes are brought into play. The effect of such forcing of the internal sphincter probably accounts for the common urgent call to micturate on getting up in the morning. Emotional stress presumably acts by stimulating bladder contractions.

Bladder dysfunction, particularly that resulting from neurological disorders, has been studied extensively, especially in America, by means of cystometry, a method first practised by Mosso and PELLACANI in 1882. This technique is an attempt to parallel the physiological filling of the bladder by slowly instilling fluid through a catheter and noting the fluctuations in intravesical pressure as registered by a manometer. A reaction to distension denoting involvement of those parts of the nervous system concerned with bladder function may be one of the earliest signs of a developing neurological lesion. Lesions of the pelvic parasympathetic nerves involving the vesical reflex arc affect the motor activity of the bladder. MCLELLAN [2] has noted significant differences, which he cannot fully explain, in the bladder changes resulting from lesions involving the posterior nerve-roots, as in tabes, and those involving both arms of the reflex arc, such as destruction of the sacral cord. In both cases sensations and reflex activity are lost, but in the former the bladder is characterised by large capacity and lack of tone, whereas in the latter it is small and hypertonic. Owing to the close apposition of the afferent and efferent spinal pathways concerned with bladder function both are commonly involved in the same lesion. For this reason disturbances of bladder sensations and impairment of cortical inhibitory control are frequent concomitants. The areas of the cortex concerned with bladder function have not been accurately defined, though according to FULTON [3] bilateral cortical lesions involving parts of areas 4 and 6, lying in the medial surface of the hemisphere, cause loss of volitional control over bladder reflexes, with urinary incontinence. The normal volitional act of micturition is said to depend on integration emanating from the hypothalamic area, as well as from the cerebral cortex. Thus, lesions of the hypothalamus cause a failure of coördination between the reflexes concerned with micturition.

The urinary incontinence which is one of the most constant and most distressing dysfunctions of the aged is discussed on another page by Dr. WILSON. In his view it is an effect of neuromuscular overactivity. Local conditions increasing the irritability of the bladder and its outlet are partly responsible for this overactivity, but impairment of cortical control, whether or not accompanied by demonstrable organic lesions, is the main factor. WILSON urges the importance of the semisomnolent state into which aged patients commonly decline when kept in bed, their inhibitory function becoming involved in the general sluggishness. Apart from the treatment of infections of bladder or vagina, WILSON treats these patients by re-educating their inhibitory function and encouraging them to lead an active mental and physical life. The probable effect on bladder function is yet another argument against allowing old people to become bed-ridden before they must.

1. Denny-Brown, D., Robertson, E. G. *Brain*, 1933, 56, 149.

2. McLellan, F. C. The Neurogenic Bladder. Springfield, 1939.
3. Fulton, J. F. The Physiology of the Nervous System. London, 1943.

Digitized by Google

Medullary Nailing

DURING the second half of the late war orthopædic surgeons in Britain and Western Europe began to encounter, among prisoners repatriated from Germany, fractures which had been treated by inserting a steel nail throughout the length of the marrow cavity. This method, originally described by KÜNTSCHER at the Vienna Surgical Congress of 1940, had been received in Germany with early coldness and later enthusiasm, and the published reports on it had been noted here with some scepticism,[1] but it was then seen to be a practical success. Now that the best part of a decade has elapsed, intramedullary nailing is routine in many German centres, where it would be unusual not to treat a fresh fracture in this way. The latest edition of BOEHLER's famous textbook[2] includes a special volume on the applications of the technique. The textbooks of SOEUR[3] and ROCHER[4] witness its adoption in Belgium and France, and WESTERBORN[5] has described results obtained in Scandinavia. But in Britain and the U.S.A. surgeons are still slow to accept it, and little more than an occasional case-report is to be found in the journals. It is not as if the principle of axial control were new. The intramedullary bone peg is an old—and usually inefficient—friend; LAMBOTTE,[6] before the first world war, experimented with the clavicle and other bones, as later did that versatile surgeon HEY GROVES. More recently, LAMBRINUDI[7] used central Kirschner wires for stabilising difficult fractures of the forearm bones. The issues may be stated somewhat as follows.

In post-war Europe, with its shortage of hospital beds and materials and lack of skilled aftercare and chemotherapy, the advent of the Küntscher nail was enormously advantageous. Patients could be sent home after a week or two, usually without plaster splintage, and often returned to light work after a month. Physiotherapy was unnecessary when, for practical purposes, the fracture had been abolished at the outset of treatment. Of BOEHLER's three famous tenets of absolute reduction, absolute fixation, and maximum function, it was for the surgeon to achieve the first, and the insertion of the right-size nail provided the second and permitted the last. In Britain and America a different situation, with a sufficiency of penicillin and good-quality metal appliances for internal fixation, accounted for the hesitant attitude towards the new method. When open reduction was necessary, vitallium plates and screws of known performance were used. Deliberate leisurely open bone operations, protected by chemotherapy and transfusion on the scale the war had made possible, still seemed promising enough to make surgeons reluctant to contemplate quite a different technique. But plates and screws have their disadvantages. They impose mechanical conditions at the fracture site with which the osteoblasts must comply or the technique will fail; and they may nullify the longitudinal compression forces essential to sound union. Hence the various stratagems—the coaptors of DANIS,[8] and the slotted plates of EGGERS[9]—designed to allow the biological element in union full play. The Küntscher nail, on the other hand, is an axial rod on which the bone fragments are threaded and which converts all the forces of weight-bearing and muscle spasm into longitudinal compression at the fracture gap.

The technique and its applications vary in different hands. Where KÜNTSCHER and his colleagues would use the nail for almost every closed fracture in adults, others reserve it for difficult cases. On p. 387 in this issue Mr. FRAENKEL describes the standard methods used at Schleswig and Kiel, where a "closed" technique is usual, the fracture being reduced by traction and the nail inserted through a stab over one end of the bone under fluoroscopic control. KÜNTSCHER himself never exposes the fracture, abhorring the periosteal reflexion and fall in local pH which set back healing; and if closed methods fail he resorts to old-fashioned traction or plaster. Other surgeons do not hesitate to perform open reduction and to introduce the nail at the fracture level by a retrograde method. At some clinics no external splintage is used, whereas at others a plaster cast gives the surgeon a good night's rest.

The clinical, functional, and economic advantages of nailing are so obvious that we may reasonably pay particular attention to its disadvantages and to the minority of failures. As MCFARLAND[10] has said—and it cannot be repeated too often—"the fracture patient should be at least no worse off after treatment than if left alone; he should be positively better treated than untreated; operation should leave him in a better state than non-operative treatment; and the added risk of operation—a real one—should be commensurate with the added benefit." The sepsis-rate in the great mass of German nailing operations is somewhere in the region of 5%,[11] a figure which, while acknowledging our own imperfections, we must regard as 5% too high. But against this, those who nail regularly regard infection as a nuisance but not a menace. It does not lead to a general osteomyelitis, and the nail must *not* be removed, for its splinting action is now doubly important and it drains the pus to the surface at the site of introduction, where simple drainage of the soft parts may be all that is needed. Fat-embolism seems to be mainly a theoretical danger, except perhaps in the femur; SOEUR records only one case where it possibly occurred. Does the nail hinder callus formation? Apparently not; in KÜNTSCHER's famous animal experiment, the insertion of a nail into an intact bone provoked ensheathing callus formation in the absence of any fracture. The question of X-ray control is a major one. The free use of screening makes nailing a rapid and trivial operation, but the hazards are too serious to be ignored. As SOEUR advises, it should be abandoned in favour of repeated radiography as for the insertion of a Smith-Petersen pin, a deliberate, often tedious, and major operation. It is obvious, too, that there

1. *Bull. War Med.* 1943, **4**, 16; 1944, **4**, 333.
2. Boehler, L. Technik der Knochenbruchbehandlung im Frieden und im Kriege. Vienna, 1944.
3. Soeur, R. L'osteosynthèse au clou. Brussels, 1946.
4. Rocher, C. L'enclouage medullaire. Paris, 1945.
5. Westerborn, A. *Ann. Surg.* 1948, **127**, 577.
6. Lambotte, A. Chirurgie opératoire des fractures. Paris, 1913.
7. Lambrinudi, C. *Proc. R. Soc. Med.* 1940, **33**, 153.
8. Danis, R. At 12th Congress of the International Society of Surgery. *Lancet*, 1947, ii, 520.
9. Eggers, G. W. N. *J. Bone Jt Surg.* 1948, **30A**, 40.
10. McFarland, B. At B.M.A. Annual Meeting, section of orthopædics. *Lancet*, July 10, p. 68.
11. Le Vay, A. D. At B.M.A. Annual Meeting, section of orthopædics. *Brit. med. J.* July 17, p. 158.

Digitized by Google

is no place for the occasional nailer, any more than there is for the occasional surgeon in any field, and the new method should be tried only at the large fracture centres in this country. It is being so tried, and the first reports will be awaited with interest. Finally, the purely orthopædic applications of the intramedullary nail must not be forgotten, for in arthrodeses, osteotomies, and bone-lengthening and bone-shortening procedures of all kinds, KÜNTSCHER has shown that it has a place of great value. Here is a field for experiment open to every orthopædic surgeon.

Annotations

PENICILLIN IONISATION THERAPY

LOCALISED infections of surface tissues are now commonly treated by simple topical applications of penicillin; but the not-infrequent failure of this method has caused the depth of penetration and degree of absorption to be questioned, and Sophian [1] has shown experimentally that tissue penetration is very superficial and absorption slight. Iontophoresis has been used in the hope of overcoming these difficulties but there have been conflicting reports on its effectiveness, and Hamilton-Paterson [2] has obtained results which seemed to show that penicillin salts are poor conductors or non-conductors of the electric current. Moreover, Popkin [3] was unable to demonstrate penicillin in the blood of patients treated by penicillin applied to the skin by iontophoresis.

Recently, Pereyra [4] has compared the specific-conductivity curves of penicillin G and crude sodium-penicillin extract with those of 'Mecholyl' (acetyl-β-methylcholine) and sodium salicylate, both commonly used in iontophoretic treatment, and with sodium chloride, a highly ionising inorganic salt. The crude penicillin was a better electrical conductor than stock sodium penicillin G, and when used in the right concentration was little inferior in this respect to mecholyl chloride or sodium salicylate. Thus, Hamilton-Paterson's inability to demonstrate conduction in his experiments may have been due to the low concentrations of penicillin employed—namely, 25–50 units per ml. Pereyra points out that 8000 units per ml. of sodium penicillin G or 5000 units per ml. of crude sodium-penicillin extract gives a penicillin concentration of 0·5%—a strength at which satisfactory results are obtained from mecholyl chloride and sodium salicylate. This concentration of penicillin is well tolerated by the skin and mucous membranes; and Pereyra found that the application of solutions in a glass chamber was more effective than by the more usual gauze-pad technique.

Absorption with iontophoresis was compared with that from ointments rubbed into the skin of the antecubital area for 15 minutes. Blood was withdrawn from the vein of the opposite arm at intervals up to an hour after treatment, and urine was collected for 2 hours. After neither inunction nor iontophoresis could penicillin be detected in the blood; in the urine, however, penicillin appeared within 15 minutes of iontophoresis. The presence of this urinary penicillin was found to depend on the application of the negative electrode only to the solution; it was estimated that the skin transference of penicillin was at the rate of about 1 unit per sq. cm. of skin per minute. The alkalinisation of the solution by the current, using 5 milliamperes for 15 minutes, caused no appreciable destruction of penicillin. To limit this alkaline shift, only distilled water should be employed for dissolving the penicillin.

The application of penicillin by iontophoresis thus offers definite advantages over parenteral and simple topical administration in the treatment of localised surface tissue infections; the concentrations of penicillin achieved at the site of application much exceed those possible by the parenteral route. This has been endorsed by Pereyra and Laudy [5] who showed that penicillin when administered parenterally fails to heal chancroid ulcers, but when applied locally by iontophoresis produces prompt remission; and a similar finding has been made by Pereyra in a series of 13 cases.

1. Sophian, L. H. *Amer. J. med. Sci.* 1944, **208**, 577.
2. Hamilton-Paterson, J. L. *Brit. med. J.* 1946, **i**, 680.
3. Popkin, R. J. *J. Amer. med. Ass.* 1946, **132**, 238.
4. Pereyra, A. J. *Nav. med. Bull., Wash.* 1948, **48**, 40.

INDUCEMENT FUND

EXECUTIVE councils have lately been seeking the views of local medical committees on the adequacy of general medical services in their areas. Account is being taken of the numbers of the population (including, naturally, those who have elected to seek medical advice privately) and of the doctors engaged in general practice as principals or as assistants, together with any local social or topographical features which might make the provision of a medical service more than ordinarily difficult.

Presumably the next step will be to try to attract extra doctors to those areas found to be under-provided. In areas where doctors' lists approach or exceed the permitted maxima, they have the choice of curtailing the acceptance of new patients or of arranging for additional assistance. In such an area a newcomer should find an immediate and growing income, which could be enhanced at first, if need be, by acceptance of the annual fixed payment. A greater difficulty, until the housing shortage has eased and health-centre building becomes possible, may well be the finding of suitable accommodation in which to practise and to live. Elsewhere, and notably in sparsely populated moorland areas, quite different factors may hinder executive councils in improving, or even maintaining, an already inadequate service. It was for such areas that the inducement payments were primarily intended; and in a timely letter the Ministry of Health reminds the councils of a fund from which such payments may be made. The money set aside for this purpose is equal to 1% of the total central pool for the payment of general practitioners, but it comes from a separate grant and is not a charge on the pool. This money is immediately available, and the Minister intends that the first payments shall, wherever possible, be made by the end of the present quarter. He therefore urges early action by executive councils, in consultation with the local medical committees, to assess and bring to his notice

"any cases where they are satisfied that general medical services adequate to the needs of the district cannot be provided, or cannot reasonably be expected to be maintained, without an inducement payment, and the amount of the inducement payment which they consider necessary to enable an adequate service to be provided or maintained."

The council is reminded that mileage payments to rural practitioners are likely to be at least double those received in the past, but that the special-subsidy portion of the old insurance mileage fund has ceased. From this fund special payments used to be made in respect of patients to whose homes access was difficult; it also subsidised heavy expenses such as those caused by the necessary upkeep of scattered branch surgeries. From now on such assistance will come directly from the inducement fund.

The Minister's letter suggests four other types of case where inducement payments will probably be needed. The first is where a vacancy has been advertised but no applications have been received; but the receipt of one or more applications for an advertised post should not

5. Pereyra, A. J., Laudy, S. *Ibid*, 1944, **43**, 189.

Digitized by Google

preclude special payments, if the executive council believes them necessary for an equitable income, or perhaps to secure a candidate better suited to local requirements. Possibly, however, this might come under the next suggested category, where a vacancy is to be advertised for an area which in the past has always attracted too few doctors. The third situation quoted is one where a doctor might be unable to manage on the income he expects to receive under the new service. This may be the plight of many a rural practitioner, whose practice, while no less arduous, is numerically smaller than that of his urban colleague. Wherever, too, the executive council considers that an extra doctor is needed, for geographical or other reasons, in a small community, it seems only fair for them to consider special payments not only for the extra doctor but also for any neighbouring practitioner whose income might be seriously prejudiced through the introduction of a newcomer. Lastly, it is suggested that special consideration might be given to the practitioner with an abnormal number of aged and chronic sick on his list, or in the parallel case of a vacancy in an area where large numbers of such people reside. Presumably this would refer to spas and similar places in which invalids tend to settle, and to towns from which, at times of industrial depression, a high proportion of the younger people have moved.

These suggestions do not preclude executive councils from putting forward other cases in which they think inducement payments should be made, though the Ministry hopes that, wherever possible, minor hardships or difficulties may be met through the annual fixed payment of £300 allowed under regulations, thus avoiding a multiplicity of claims on the inducement fund. All proposals from executive councils "will be referred by the Minister to the Medical Practices Committee for advice on the payments to be made in individual cases within the total sum available for distribution for inducement payments." Each year the executive council, in consultation with the local medical committee, will review all payments approved by the Minister and report on the need for their continuance. Hardship will sometimes not be evident at once; in fact, it may not become obvious, even to the doctor himself, until the numbers of patients on practitioners' lists have been agreed and the first quarterly payments made. But it should not be difficult, if authority allows, for the Medical Practices Committee to sanction immediate interim payments to the more obviously needful, while keeping enough in reserve to make retrospective payment to doctors whose needs declare themselves later.

HISTAMINE FOR MIGRAINE

BOTH histamine and anti-histamine drugs have been recommended in the treatment of migraine. Butler and Thomas [1] were enthusiastic advocates of the former, which they administered intravenously by a rather elaborate technique. Cautious-minded readers of their original papers may have been impressed more with the duress of the régime than with the benefits accruing from it. Histamine has been used in migraine at the Mayo Clinic since 1937, and Macy and Horton [2] have lately assessed their results, carefully excluding instances of what they term "histaminic cephalalgia." [3] The cases of migraine, numbering 144, were divided into two groups: (1) 124 treated with histamine only, whether subcutaneously, intravenously, or both; and (2) 20 treated by the original Butler-Thomas technique, with intravenous injection of a 1 : 500,000 solution of histamine base, coupled with epinephrine and ascorbic acid. It proved difficult to judge the efficacy of the drug. Macy and Horton rightly remark that migrainous subjects are particularly liable to headache of other types, which will lower the threshold for an actual attack of migraine; but they believe that confusion from this cause is avoidable. They found that in 23–33% of cases the syndrome was unchanged by histamine, irrespective of the route of administration. About 60% showed significant improvement, which was apparently most pronounced with combined subcutaneous and intravenous injections. But of 88 patients whose condition was improved, 85 had a recurrence when the histamine was reduced or discontinued. The authors cautiously conclude that "histamine may prevent some attacks of migraine in some cases." In their opinion histamine, though neither a specific nor a truly curative agent, will continue to have a place among the prophylactic measures against migraine.

1. Butler, S., Thomas, W. A. *J. Amer. med. Ass.* 1945, **128**, 173; *Amer. J. Med.* 1946, **1**, 39; *Bull N.Y. Acad. Med.* 1946, **22**, 125.
2. Macy, D. jun., Horton, B. T. *J. Amer. med. Ass.* 1948, **137**, 1110.
3. Horton, B. T., MacLean, A. R., Craig, W. M. *Proc. Mayo Clin.* 1939, **14**, 257.

INFECTION BY TRAIN

THE pollution of railway tracks by excreta from train closets has not yet received as much attention in this country as it has in the United States, where the joint committee on railway sanitation set up by the Association of American Railroads has recently sponsored a great deal of careful research with the coöperation of the United States Public Health Service and the epidemiological department of the Johns Hopkins school of hygiene and public health at Baltimore. The results of these inquiries have been published in a series of special reports, of which the most interesting is that by Maxcy,[1] who made an exhaustive survey designed to find out how far polluted railway tracks were a cause of the spread of disease and in particular of enteric fever. After a special study of exposure to this source of infection through residence in proximity to railway tracks, employment on such tracks, or the consumption of water-supplies which might be polluted by railways at some point in collection and distribution, he could not establish the existence of a danger to public health from the method of disposal of fæcal wastes employed by railways. The further studies, summarised by Wolman and Clark,[2] are mainly quantitative, being based on observation of the toilet habits of 2000 persons travelling 320,000 miles by train during 6261 passenger hours. Excreta from these persons were collected in sealed containers carried underneath the coaches, and it was found, for instance, that along the 226 miles between New York and Washington about 0·694 lb. (dry weight) of sewage solids were being deposited per yard of track per year.

The construction of the closets in British trains and the habits of the passengers using them are probably sufficiently similar for the American results to be roughly applicable over here. As Mr. Chapman Pincher [3] pointed out last year, the potential dangers of current railway practice are obvious, but hitherto in Great Britain, as in the U.S.A. there has been hardly any evidence of the spread of disease by this means. Pincher suggested that poliomyelitis was being spread in this way, but among the many accounts of the large number of local outbreaks which made up last year's epidemic only one [4] has mentioned the residence of cases in proximity to main-line railway tracks. However, in this particular outbreak, in a London borough, the distribution of cases was very striking. The main line carrying ships' passengers from Tilbury Docks to St. Pancras station passes through Tottenham on a high and exposed embankment, whereas thereafter it runs through Islington in a cutting. At Tottenham,

1. Maxcy, K. E. Technical Report no. 2, Joint Committee on Railway Sanitation of the Association of American Railroads. New York, 1946.
2. Wolman, A., Clark, L. K. *Amer. J. publ. Hlth*, 1948, **38**, 652.
3. *Lancet*, 1947, ii, 370.
4. Broadbent, B. *Med. Offr*, 1948, **79**, 274.

Digitized by Google

all but one (a doubtful case) of the 17 confirmed cases were in people who lived—or in one case worked all day—within a quarter of a mile from this railway. In Islington, on the other hand, the incidence was low and there was no such aggregation of cases near the railway. It seems reasonable to argue that incoming travellers from abroad would be likely to include a particularly high proportion of carriers of poliomyelitis; and also that virus in their excreta, deposited from the train closets, would be more readily air-borne from the top of an embankment than from the bottom of a cutting. This one example cannot be considered proof of the hypothesis, but it should spur on the Railway Executive to reconsider the arrangements for the disposal of human excreta on their trains. The sanitary engineer who designs an inexpensive device which will collect and contain train sewage during the journey and which can be rapidly emptied into a sewer at the end of the run should be assured of a handsome reward.

JUVENILE OSTEOCHONDRITIS OF THE SPINE

CHILDREN with the disorder described by Scheurmann [1] as kyphosis dorsalis juvenilis seldom make any complaint; yet many are deformed, with irregularities of ossification of the vertebral bodies; and later, under stress or strain, these changes can give rise to pain. The evidence suggests that this condition of juvenile osteochondritis is at least partly instigated by malnutrition during growth, and that benefit can result from an improved dietary.[2] In this country the worst cases have been observed among the younger members of large families in certain Oxfordshire villages where wages were low before the late war, and where severe dental fluorosis is also found among the inhabitants. In the occasional cases seen in children from the higher income groups there is a history of long-continued ill health or feeding difficulties. The geological distribution of cases indicates an association with some factor closely related to fluorine, a trace element which may itself interfere with enzyme systems concerned in the calcification of bone.[3]

Kemp and his colleagues,[4] in an investigation of the ætiology of Scheurmann's disease, compared two groups of boys—the first from a public school and the second from the poorer quarters of Oxford. Some of the boys in the first, and presumably better-nourished, group had dental fluorosis, whereas none of the second group, who were not exposed to a high fluorine intake, were thus affected. Both these groups were compared with a third, living in a village community where dental fluorosis affects nearly all the inhabitants and considerable poverty formerly prevailed. In this group spinal changes were more than three times as common as in the other two groups, and the disturbances were in some instances more severe. Although spinal changes are not always found with dental abnormality ("mottled enamel"), the probability of spinal changes in a community can be gauged with fair accuracy by examining the teeth. The investigators conclude that in view of the association recognised in other countries, of endemic dental and osseous fluorosis with malnutrition, the possibility of a similar association between dental fluorosis and juvenile osteochondritis must be borne in mind.

Whatever the intimate pathology of the disease, the practical implications of these findings are evident. Probably even the most severe cases could be prevented by a good dietary; and special attention should be given to children living in rural areas, particularly where dental fluorosis is prevalent. Thus a condition hitherto regarded as chiefly the concern of the orthopædist is in all probability completely preventable by proper nourishment.

1. Scheurmann, H. *Z. orthop. Chir.* 1921, **41**, 305; *Fortschr. Röntgenstr.* 1936, **44**, 233.
2. Kemp, F. H., Wilson, D. C. *Brit. J. Radiol.* 1947, **20**, 410.
3. Murray, M. M., Wilson, D. C. *Lancet*, 1946, ii, 821.
4. Kemp, F. H., Wilson, D. C., Emrys-Roberts, E. *Brit. J. soc. Med.* 1948, **2**, 66.

HOSPITAL LIBRARIES

MANY doctors regret that they have not more time for professional reading. What time they have can be used best if textbooks and journals are within easy reach. Group practice enables some to have a selection of books at hand; and a similar advantage will be gained from health centres. Here and there the general practitioner finds a hospital where he is welcomed to a reading-room.

The reorganisation and grouping of hospitals opens the way to a better-organised library service; and management committees will now have to decide on the resources to be offered to their staffs. There seems to be need for a general policy, particularly in view of the continuing shortage of textbooks. In the past some local authorities took the view that their medical staffs should provide their own books; but then the cost was much less than now, and committees will certainly be called on to review this decision. Any provision will have to be made on a group basis since the supply would soon be exhausted if every hospital had even £50 to spend on books and journals. Perhaps it will be possible to enlist the help of the public libraries, which are increasingly used by serious readers and those needing books of reference, whether in commerce, industry, or the professions. Possibly each group of hospitals should aim at a centralised library, stocked in conjunction with the public library and staffed under its auspices, since the value of a library largely depends on the efficiency of the librarians. Management committees also have obligations to other members of hospital staffs. In particular, the nurses and other auxiliaries need a professional library, and if the public library is not readily accessible provision should be made for their recreational reading; a subscription to a commercial lending library is hardly enough to ensure a tempting selection. At least one public librarian, with the cordial consent of the hospital committee, has arranged to supply and staff a hospital library to meet the needs of each section of the staff and the patients. The Minister of Health has drawn the attention of management committees to patients' libraries as a medium for continued voluntary work within the hospital; but many voluntary librarians realise that the efficiency of their work would be considerably enhanced by coöperation with the public librarian. This alliance benefits patients by helping to meet their special requests, which tend to cover an increasing range. In long-stay institutions such as sanatoria and mental hospitals there is particular need for a comprehensive service; and the example set by Crichton Royal has already been followed by another large mental hospital, which has established in its grounds a branch of the county library.

The extension and integration of such a scheme requires a good deal of planning: the areas of the hospital service do not coincide with those of the library authorities; resources may be available in one place and not in another; and librarians may find it hard to undertake additional work which may make considerable demands. Clearly the regional boards will need a professional adviser to plan for the whole region; and he will hope to find in the medical-school librarian a sympathetic professional colleague; since the Goodenough report was published, the medical schools have shown greater readiness to appoint trained librarians. If, as the B.M.A. curriculum committee [1] suggests, "the library is indispensable and the student must be guided in its use, so that in his later professional life he will have in it a constant ally and friend," then a professional librarian is an essential member of the staff.

1. Training of a Doctor: Report of the Medical Curriculum Committee of the British Medical Association. London, 1948; para. 93.

Digitized by Google

Special Articles

INTRAMEDULLARY NAILING OF FRACTURES

THE PRACTICE AT KIEL

G. J. FRAENKEL
M.A., B.M. Oxfd, F.R.C.S.
SURGICAL REGISTRAR, GENERAL HOSPITAL, NOTTINGHAM

I HAD heard of Küntscher's method of intramedullary nailing intermittently during the later years of the recent war from British, Swiss, and Dutch surgeons. The remarks of the British surgeons had been unfavourable, those of the Swiss and Dutch very favourable. As I had seen no account of the method in the more widely circulated British journals, I was unable to study it until I visited the University of Kiel last year, where Prof. Gerhard Küntscher first practised this technique, and where Prof. H. Griessmann and Dr. Richard Maatz kindly showed me the method, operations, results, and literature. I am not in a position to assess the value of the method with any authority, but some of my colleagues may be interested in what I saw of it.

The principle of intramedullary fixation is old, and no novelty is claimed for it. The present method is an extension of the principle of the Smith-Petersen nailing of fractures of the neck of the femur to fractures of almost all long bones, and was presented by Professor Küntscher to the Chirurgen-Kongress in Berlin in 1940; it was received very unfavourably by his German colleagues, who, however, became enthusiastic about it shortly afterwards.

The basis of the method is that a long slightly flexible stainless-steel nail, approximately V-shaped in cross-section, is introduced into the marrow cavity of the fractured long bone from near one end; then, after anatomical reduction of the fracture by manipulation, the nail is driven across the fracture site, under radioscopic control, into the other fragment sufficiently far to secure absolute immobilisation. In a suitable case no additional immobilisation is required, and thus there is no loss of function or joint stiffness. The nursing of a patient with a fractured femur, for example, is much easier, and his general health far better, than during immobilisation in a Thomas splint. Further, the physiological stimulus of function is conducive to early and firm union, and muscle wasting is diminished.

The method has been applied to simple, compound, and pathological fractures, and for immobilisation in arthrodesis, osteotomy, and the treatment of pseudarthroses.

The only essential requirements for nailing are an X-ray plant suitable for screening (the apparatus at Kiel is superior in point of smallness and mobility to any I have seen) and an assortment of nails of suitable sizes. At Kiel the nails are made locally by the hospital instrument-maker, and a suitable nail is selected by measurements on radiograms incorporating a scale. If there is no suitable nail in stock, the instrument-maker manufactures one, usually in less than 24 hours (other hospitals telegraph for them). It is important that the nail should not be too thick, because such a nail can become so firmly wedged at the "waist" of the bone as to cause the greatest difficulty.

The first essential is perfect reduction. At Kiel this is achieved with blocks and pulleys and, in special cases, skeletal-traction wires and other mechanical apparatus. The reduction is checked by very brief screening, a small incision is made over the site of entry of the pin, and the cortical bone is pierced to the marrow cavity. Either the guide pin or the nail (see below) is then introduced into the marrow cavity and propelled along it, a further brief view on the screen being taken as it crosses the fracture line. In the case of a guide pin the nail is now threaded down and the pin withdrawn, the small incision is closed, and check films are taken. The operation usually lasts about 10–20 min. and is carried out under 'Evipan,' spinal, or brachial block anæsthesia.

The necessity for screening is a major drawback. This is realised, and the most stringent precautions are taken. The danger of sepsis appears appalling at first, and yet it has given rise to practically no trouble, though penicillin has not been available for any of these cases. The danger of fat-embolism also has been found to be entirely theoretical. Though it undoubtedly must occur, no clinical effects have been observed.

The following details are extracted from a careful analysis [1] of 155 cases nailed at Kiel from Jan. 1, 1944, to May 1, 1946—i.e., during the time of the worst chaos there (the clinic stands in acres of rubble and was hit frequently).

Femur

Subtrochanteric fractures are very satisfactorily controlled with a short special nail (fig. 1).

Shaft (fig. 2): a guide pin is usually employed, and it or the nail is of help in manipulating the upper fragment.

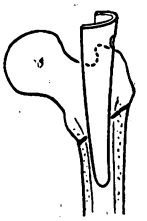


Fig. 1—Special nail for subtrochanteric fracture of femur.

Supracondylar fracture: the nail is of great value in preventing angulation, but additional immobilisation is required because of the width of the marrow cavity.

In all these cases the nail is introduced just medial to the greater trochanter.

Of 35 simple fractures 27 were stable; the others required additional immobilisation, but angulation was absolutely prevented. In stable cases the patients started walking in 7–42 days. Two patients with associated multiple injuries died; operation was an error of judgment. All others were symptom-free after $3\frac{1}{2}$ months. No nails were removed before 4 months. Of 7 compound fractures 3 were stable without additional immobilisation, all united, and only one case with gross loss of soft tissue had loss of function.

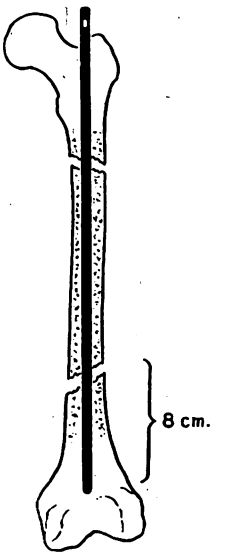


Fig. 2—Nailed fracture of shaft of femur.

Four pathological fractures were nailed and irradiated, and 2 osteotomies nailed, with excellent union.

Tibia

Owing to the hourglass shape of the marrow cavity a special double nail is inserted from the region of the tuberosity or of the medial malleolus (fig. 3). The first nail carries a wedge which forces away from it the following second nail, thus securing the lower end firmly.

Of 46 simple fractures all those put up with the double nail were stable; but 10 nailed with a single nail because of multiple fractures which the double nail could not pass, or for other reasons, required additional plaster. Even in these cases the position was far better than could have been otherwise achieved. One patient died in the 5th week of other injuries; 1 aged 81, with a fractured femur also, died of pulmonary embolus and bronchopneumonia. All others had a good anatomical and functional result. No nails were removed before 3 months, and there was difficulty in extraction in 2 cases. Of 15 compound fractures 14 were stable. One patient died of pulmonary embolus in the 3rd week; and 1 died of multiple injuries and shock (air-raid casualty). Two pseudarthroses united after freshening and nailing.

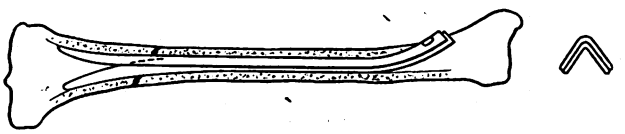


Fig. 3—Double nail for fractured tibia.

Humerus

This can be nailed with ease from below or above (figs. 4 and 5). The early and full function of arm and hand is remarkable.

Ten closed fractures (7 nailed from above, 3 from below) were all stable and achieved good union with full function. Nailing of 2 pseudarthroses with freshening led to firm union. In a compound infected fracture with multiple injuries which

1. Griessmann, H., Schüttemeyer, W. *Chirurg*, 1947, 17-18, 316.

Digitized by Google

was nailed in the 4th week there was anatomical union after sequestrectomy. In a pathological fracture (carcinoma of bronchus) nailing brought about good function.

Radius and Ulna

The radius is nailed from the lower end, and the ulna from the upper end (fig. 6). The stability of this method of fixation offers great advantages here, but reduction may be difficult.

In 16 closed fractures open reduction had to be used in 6 cases (difficulties of reduction would be the same whatever the method of immobilisation). All united well except that of a workman who started heavy work 4 weeks after injury

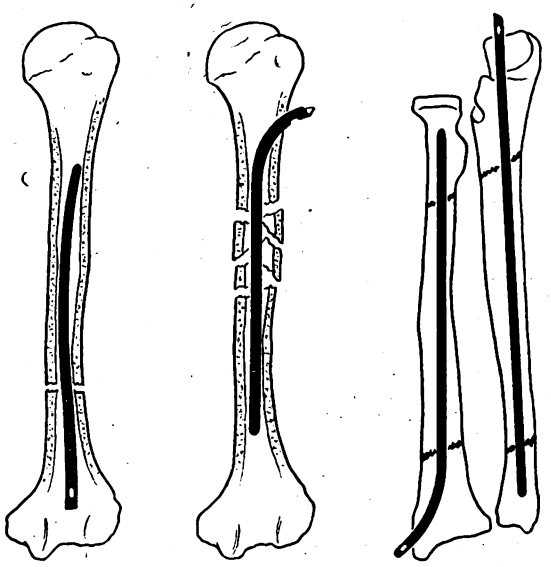


Fig. 4—Fractured humerus nailed from below.
Fig. 5—Fractured humerus nailed from above.
Fig. 6—Fractured radius nailed from below, and fractured ulna nailed from above.

(without medical consent), broke the nail, and developed a pseudarthrosis of the ulna. This united after extraction of the nail fragments, freshening, and renailing.

Nails were left in for at least 3 months.

Two compound fractures were nailed and united well; in one a defect of 4 cm. in the ulna was bridged by bone without grafting.

My impression is that the advantages derived from the early and anatomical union, and from the full joint and muscle function preserved throughout, outweigh the disadvantages, which are mainly the necessity for a moderate amount of apparatus and for screening. The dangers of sepsis and fat-embolism appear to be largely theoretical, and there is ample evidence that the nails have no adverse effect on bone or marrow.

I am, however, not competent to pass an opinion, and merely advocate that the method should be studied far more widely than appears to have been the case so far.

The accompanying figures are based on those of Küntscher and Maatz,[2] whose monograph should be consulted for further technical details.

2. Küntscher, G., Maatz, R. Technik der Marknagelung. Leipzig, 1945.

"... Upon the limited soil of this planet we have to produce the food for an increasing population. There is no chance of importing supplies from Mars or the Moon. We might as well face the problem calmly and agree that we have of late years made an unholy mess of our solutions. The fault does not lie with the producers of food, who are a vast dispersed multitude of farmers and peasants. The fault lies rather with ourselves as social beings, in that we have given too little attention to what our scientists and economists were attempting to tell us. . . . We should by this time be thinking of food production and food distribution in the world as problems in good management; and many of our statesmen are obviously still thinking of them in terms of 19th century nationalism or imperialism."—F. LE GROS CLARK in *Feeding the Human Family*. London, 1948.

INTERNATIONAL CONGRESS ON POPULATION AND WORLD RESOURCES

THE International Congress on Population and World Resources in Relation to the Family, arranged by the Family Planning Association, was held at Cheltenham from Aug. 23 to 27. Like the recent Mental Health Congress this gathering ended its deliberations by forming an international body. For the present it takes the form of a provisional international committee to promote research and education in family planning, with two representatives from each of the national organisations in the U.S.A., Great Britain, Holland, and Sweden, and such individuals from other countries as they coöpt. The secretariat will be in London.

Sir JOHN BOYD ORR, F.R.S., opening the congress, stated the crux of the discussion: if we cannot solve the problem of world resources in this century, we are heading for the greatest catastrophe in history. Before the 1939–45 war two-thirds of the world population were not fed, clothed, or housed up to a basic level of necessity. The world population is increasing by 20 million a year. Before 1939 it was 2000 million; at the end of the century it will be 3000 million. To feed these people food production must be doubled within the next 25 years. When standards of living rise the birth-rate falls; and the only way to get a static world population is to raise the standard of living and education. It was 150 years to the day, he said, since Malthus published his famous pamphlet prophesying disaster from over-population; but Malthus did not foresee the opening up of the southern hemisphere as a source of food. Now we have no new hemispheres to rifle, and much of our land is losing its fertility; dust bowls have been created, and soil erosion means a falling reservoir of food resources. Some hold that it will not be possible to provide food for all, but in Sir John Orr's view if all cultivated land is brought up to the level of the best the same production will be possible with half the acreage. Moreover it should be possible, by irrigation and reafforestation, to recover land which has become barren. We have not yet explored the resources of timber, which can provide food, textiles, and other essential commodities. Sir John believes we can feed and shelter the population likely to be achieved in the next 150 years; and indeed that the total number the world can feed is only limited by the amount of attention governments give to the problem. In the view of Malthus, the excess population should be allowed to die out; but he ignored the fact that people will not die quietly. They will fight, as they were ready to do in England in the hungry 'forties. We must have a world plan for food.

Dr. ABRAHAM STONE (U.S.A.) pointed out that so far more food has always meant more population. To improve food production is not enough: we must also disseminate the means for family planning.

ESSENTIAL STANDARDS OF LIVING

Prof. FRANK LORIMER (U.S.A.) thought that to make it possible for another thousand million just to keep alive would not make for peace. Malthus failed to allow for the rôle of experimental science in raising food production, and for the effect of a rise in the standards of living. The more fortunate peoples—about a fifth of the world's population—were getting at the beginning of the late war 2875 or more calories per person per day. These included all the peoples of Western Europe, Australia, New Zealand, and the American countries north of the Rio Grande and south of Brazil and Cuba. Another 30% of the world population—in southern and eastern Europe, Soviet Russia, Brazil, Paraguay, Chile, Japan,

Digitized by Google

Manchuria, Burma, Malaya, and parts of Africa—lived at intermediate levels, getting 2500–2875 calories; while the remaining 50%—about a thousand million in eastern Asia and middle America and in a large part of Africa—got less than 2500 calories. The low-income countries have a high fertility, and as long as this fertility is maintained every modern improvement which leads to a reduction in mortality leads to a spurt in population growth. The rice economy, on which millions of people depend, is peculiar. There is scarcely any other method of production capable of yielding so many units of food energy per unit of cultivated land as paddy growing, and it can be doubled by the use of fertilisers and selected plants. Conceivably it might be increased rapidly enough to outstrip the needs of the growing population, but this is doubtful. We must, in short, find more rapid means of reducing human fertility. An improvement in standards of living, new methods in agriculture, and the introduction of planned parenthood are all complementary measures.

Dr. H. M. SINCLAIR also emphasised the gain in food production which could be expected from better agricultural methods and the control of infestation, and by extending cultivation to new areas. He touched on some new methods: cultivation of soil-less plants, and the synthetic production of fats from carbon monoxide and steam.

Dr. A. M. DURAND-WEVER (Germany) said that in the Russian Zone and in Berlin Germans have been living on 1200–1800 calories daily for the last three years. The quality of their food is poor, with shortage of fats and proteins and no fresh fruit and vegetables. The birth-rate before Hitler, in 1933, was 8·7 per 1000; at the height of the Hitler propaganda it rose to 14·9, and is now down to 9·2. The death-rate was lowest in 1938, at 5·8 per 1000. It rose to 55 after the capitulation and is now 16.

Mr. ROY WALKER remarked that we shall soon have to feed more people than can possibly be fed at the level at which people are now trying to feed themselves. A diet meeting all requirements is provided by wholemeal bread, fruit, vegetables, and milk; and to produce such a diet $^3/_{10}$ of an acre per head suffices, instead of the $2^1/_2$ acres per head needed when animal food other than milk is taken. On such a vegetarian diet the world could get by immediately.

POPULATION TRENDS

Prof. P. K. WHELPTON (U.S.A.) pointed out that in northern and western Europe and in the U.S.A. much smaller gains in population are to be expected in the next century than in the last. The large rise in birth-rates in these countries since the war does not imply a trend towards larger families: the increase is mainly in first births. In India, China, and elsewhere, the birth-rates and death-rates are high, and western improvements in sanitation and medical care may be expected to lower the death-rate before the birth-rate falls. These areas are potentially in the "swarming" stage, as England was at the time of the founding of her colonies. In the U.S.S.R. the position is intermediate: the death-rate has been materially reduced, but the birth-rate has fallen to a lesser degree. Industrialisation of areas which now live by manual labour will raise standards of living, while further increase of population in these areas will tend to have the opposite effect. These problems would be simplified if the probable decline in death-rates could be accompanied by a greater decline in birth-rates. Simpler and less expensive methods of birth-control may come from the research programme of the committee on human reproduction of the National Research Council in Washington.

Dr. C. P. BLACKER classed population states into five stages: (1) the high stationary stage with a high death-rate and a high birth-rate; (2) the early expanding or "swarming" stage, when the death-rate is falling and the birth-rate still high; (3) the late expanding stage, in which the birth-rate is falling, but the death-rate falling faster (the U.S.S.R. is now in this phase); (4) the low stationary stage, when the net reproduction-rate is at unity; and (5) the declining phase. The crucial question is whether the nations can pass through stages 1, 2, and 3 to 4 without swarming and outstripping world food-supplies.

MIGRATION IN THE ADJUSTMENT OF POPULATIONS

Prof. T. H. DAVEY said that in the past migration had played an important part in adjusting national populations during expansion. France, on the other hand, has allowed immigration of foreign labourers to balance their excess of deaths over births. Nations in Blacker's second and third phases are liable to reach the population pressure which might seek relief in migration; and certainly urbanisation and emigration helped Great Britain to survive the rapid population expansion at the time of the industrial revolution. The overcrowded peoples of India, China, Japan, and the Dutch East Indies have no wide area of unused cultivable land. Of the appropriate countries to receive them only Australia and Canada have a stable population, and neither is willing to accept them. Moreover, though migration would reduce population in the sending countries for a time, the effect would be to reduce the death-rate and increase the rate of population growth until numbers were the same as before. In general, then, there is nothing to be hoped for from migration.

FAMILY PLANNING IN VARIOUS COUNTRIES

Dr. A. W. LANGEHEINE (Germany) said that before National Socialism family planning and marriage guidance were well advanced in Germany. In the early years of Hitler's rule contraceptives were still allowed but abortion was punished, and effective propaganda was used to encourage childbirth. Soon after 1939 a police order, later made law, forbade the use of contraceptives, and capital punishment was threatened for repeated abortion. These laws (capital punishment apart) have not yet been fully abolished, largely owing to the intervention of the Catholic countries, though general opinion is strongly in favour of their abolition. There has been a great increase in abortions; official figures of treated cases suggest a rate of 1 abortion for every live birth.

Dr. DURAND-WEVER recalled that in Germany in 1934 a secret order required soldiers to beget children wherever they could; and later the labour camps for young girls were deliberately put near those of the men. Since the capitulation of Germany marriage-guidance bureaus have been established throughout the Russian Zone in all the large cities, and 4 contraceptive clinics have been set up in Berlin. Abortion on therapeutic grounds is allowed.

Lieut.-General KIN CHEUNG (China) said that there has never been an adequate census in China, but the population is thought to be some $463^1/_2$ million. If the standard of living is to be raised the population must be reduced. The only other way to increase national wealth is by industrialisation. Chinese intellectuals have been advising birth-control since 1919.

Dr. JEAN SUTTER (France) said that in France all contraceptive measures and propaganda are prohibited at present, on pain of fine or imprisonment. This attitude

Digitized by Google

is governmental rather than ecclesiastic, and is called forth by the stationary population. England and Wales, Italy, and Germany are now following the demographic cycle in which France has been the pioneer.

Dr. G. NYCANDER (Sweden) said that the birth-rate reached its lowest point in his country in 1933, but has now recovered again. In 1946 abortion was legalised for conditions liable to endanger the health of the mother, and in cases of rape. In 1945 sex education was finally begun in schools.

Dr. P. A. VAN HUET (Holland) said that though the population of Holland had trebled in the last hundred years, and though the death-rate was the lowest in Europe, the Roman Catholic Church worked against contraception. There are legal penalties for publishing anything on the subject. Nevertheless centres have been opened and deal with both family planning and subfertility. In 1946 the Netherlands Society for Sexual Reform was founded, and has set up marriage schools for young people.

Dr. F. POLASEK (Czechoslovakia) noted that there has been a steady increase in the birth-rate of his country since the 1914–18 war. Government policy encourages this by tax remission, free antenatal and maternity care, priority in housing, and free medical treatment of infertility. There are no legal restrictions on contraception but the practice has never found much support. The government aims at a further increase of the birth-rate and the reduction of illegal abortion.

Dr. J. N. KHOSLA (India) said that the death-rate, though high (22 per 1000), has fallen. Polygamy, though permitted, is little practised, since women number only 93% of the men. He felt sure Indian women would respond as well as any other women to social change, but they have had very little sex education. Religion, he said, plays no part in the regulation of social affairs in India, but social customs do.

Prof. M. LANVAL (Belgium) observed that in his country birth-control was listed with things dubbed obscene; so anyone interested in family planning is now stigmatised at the outset. However, the law only prohibits the selling of contraceptives and the giving of contraceptive advice for profit, so doctors can give advice free—and appliances, too, if they can find a chemist who will sell them at face value.

Mr. F. M. MANSOUR (Egypt) gave two reasons for the large families of Egypt: as a sort of insurance (because infant-mortality is high and surviving children mean an easier old age); and as a hobby (because a family is a great source of interest and pleasure when there is not much other entertainment going). If the Egyptian population is to be restricted there must be a revolution in the means of production by industrialisation.

Dr. OKU AMPOFO (West Africa) said that at the start of the century his part of the world had emerged from the results of the slave-trade and was adjusting itself to European occupation. The native population in the Congo had been reduced by slavers from 8 million to 1 million. Commerce, however, has meant a change in the standard of living; and now children are becoming a liability because of the high cost of living and education. Feeling is tending towards small families and the abolition of polygamy.

BIRTH-CONTROL AND POPULATION

Dr. NILS NIELSEN (Sweden) said that birth-control alone cannot be responsible for the falling birth-rate in western Europe and elsewhere. Swedish population statistics, which date from the beginning of the 18th century, show a slowly declining death-rate and at first a high birth-rate; later the birth-rate began to fall in the towns and afterwards in the country. After 1910 the rate fell until the early 'thirties, since when there has been a small but rapid rise. It is a common custom of the country not to marry until after the birth of the first child, and not always then—indeed, about half the adult population is unmarried—so the extramarital birth-rate is always high. Paradoxically, little birth-control was taught until the birth-rate decline was in full swing. Birth-control may be potentially dangerous to a race, but extreme limitation of family is caused by economic factors and must be corrected by economic reform.

Dr. STONE talked of the remarkable change in the U.S.A. since the time, 25–30 years ago, when Mrs. Margaret Sanger started her campaign for family planning. All the Churches have recognised the importance of family planning for the stability of the family, though they may differ on methods. The law has been redefined so that it no longer offers a barrier. The medical profession have recognised birth-control as a therapeutic measure, and give instruction on it in the medical colleges. In 5 States birth-control advice is included in the public-health service, and it is hoped that in time such advice will become a part of the Federal Public Health Service.

Mrs. M. A. PYKE said that in Britain more than half the local authorities now give contraceptive advice to any woman who needs it on medical grounds. It is hoped that in the end family planning will be an integrated part of the public-health service, but for the present it works well as a combination of voluntary and official effort. The Family Planning Association undertakes much research into contraception and subfertility.

Dr. S. CHAUDRASECCA (UNESCO) said that population problems have always been a factor in causing wars. UNESCO is starting research projects on population in relation to various countries.

Miss MOYA WOODSIDE (U.S.A.) noted that in North Carolina there was a law allowing voluntary sterilisation on medical grounds for psychosis, epilepsy, and mental defect. This is, in fact, being extended widely, unofficially, to include women with large families.

ADVANTAGES OF FAMILY PLANNING

The Rev. JOSEPH MCCULLOCH said that contraception has only recently been rescued from evil associations. Family planners, however, are only concerned with those who oppose contraception for married people. These fear that mankind will end in race suicide, and that birth-control encourages the pleasure principle and irresponsibility. Such views are based on an uncompromising estimate of man's unredeemed nature. Family planning must be taught as a true fulfilment in a personal relationship. The way of redemption is by a raising of the individual level of moral responsibility. Man is born to know more and more what he is doing.

Mr. KENNETH WALKER, F.R.C.S., remarked that family planning relieves the mother of the danger to health and life produced by an uninterrupted series of pregnancies. It is preposterous to suggest that the chief motive for spacing a family is a desire for luxury. Fear of impregnating his wife, when the family is already as large as he can afford, may make a man impotent.

Dr. C. VAN EMDE BOAS (Holland) wondered why family planners were always relieved to hear an ethical defence

Digitized by Google

of their work. They should rather ask why others have failed to undertake such a plain duty.

CURRENT RESEARCH

Dr. EARL ENGLE (U.S.A.) indicated some possible lines of research on semen. The spermatozoon emerges from the testis with a complete store of energy, but it is also capable of metabolism. On an average, 100 million spermatozoa must be present if an egg is to be fertilised. The state of the cervical plug of mucus is also a factor in fertilisation. This mucus is hygroscopic, and its state is under the control of œstrogens, so that at times it becomes more fluid and thus more readily permeable.

Dr. JOHN ROCK (U.S.A.) favoured teaching young people family planning rather than encouraging them to think of the drawbacks of babies. Fertility is highest in the early years; and people are apt to use contraceptives in these years and then to ask the gynæcologist to help them to get a child in the infertile years. In the U.S.A. it is found that only people who have had less than 4 years of education replace themselves in the next generation; college graduates have not replaced themselves since 1860. One way of interfering with the reproductive cycle is to use hormones to stop ovulation for a time.

Prof. F. A. E. CREW, F.R.S. said that fertility genes are demonstrable in living forms other than man, and human pedigrees suggest that they are present in man too. Some genes are lethal and slay the individual before he has time to reproduce. Hæmophilia, for example, kills the homozygous fœtus in utero, and shortens the life of the male. The higher the species, and the longer lived and the larger the animal, the fewer the offspring. The human female is not well equipped to produce more than four young in all; and from the child's point of view all the evidence goes to show it is a bad business to be the first child and a serious mistake to be the fifth, sixth, or seventh.

Dr. MARGARET HADLEY JACKSON said that the emphasis at the congress had been on expanding populations and diminishing food, and little had been said about the encouragement of families. We belong, however, to a country in which the curtain is about to fall on the fourth act of Dr. Blacker's demographic drama. It may be that a different method of approach is needed in different areas of the world.

* * *

The congress urged the governments concerned to take all possible steps to help the occupied countries to re-establish their former organisations for planned parenthood.

". . . We are assured by Dr. Ernest Jones that a constitutional monarchy uses for the good of the State impulses and tendencies that are deeply buried within the human mind. Human beings crave for the protection of a lofty and consecrated parental figure. Their attitude towards this figure is ambivalent; but the constitutional system provides them with the beloved good parent who is the sovereign, and the potential scapegoat parent who is the Prime Minister. So far Dr. Jones. Matriarchal rule goes one step further. It removes the possibility of rivalry towards the parental figure by mobilising on its behalf the need for maternal warmth and affection. To translate this into everyday language: a female ruler calls forth deeper loyalties and chivalrous devotions, it kindles in the subject a desire to defend and to protect, instead of leaving him possessed with the sole desire of being defended and protected."—G. J. RENIER, *Manchester Guardian*, Aug. 30, 1948.

In England Now

A Running Commentary by Peripatetic Correspondents

ANY mug can wangle staphylomycin out of the Ministry for a pulmonary case, said our registrar. By the time you've read the third page of the patient's notes the tired bloke at the Whitehall end of the telephone more or less insists on sending you a month's supply. Of course, if its non-pulmonary you've got to give the Whitehall bloke some "cover," as he calls it—say that the patient is writing a personal stinker to the Minister, or that the *Daily Largesse* has offered to fly you the stuff forthwith. If the worst comes to the worst you can fall back on what was left over from the last case of meningitis.

What mugs these registrars must take us for, said the staphylomycin M.O.(supplies) moodily. By the time they reach the third page of notes on a case in which they obviously haven't done a bronchoscopy I usually chip in and say there's nothing doing until they have. Then the blackmail starts. Either the patient is writing a personal stinker to the Minister or else the *Daily Largesse* has been sniffing round. What sometimes does get my goat is the airy fairy way in which they finally say that they suppose after all they'll have to go to the black market for it as they do for their private patients.

* * *

Having duly warned the opposition that our team contained three schizophrenics and a manic, we lost the toss and went out to field. The game resembled cricket for the first ten minutes. Then one of our opening bowlers, having spent his morning in the depths of an insulin coma, had his usual hypoglycæmic reaction after the fourth ball of his second over. We were by now able to recognise the onset in the prodromal stages as the usual symptoms were ushered in by a succession of wide full tosses and long hops. These derived from his diplopia, and, while the sight of six stumps instead of three might have been expected to increase his confidence no end, they were unfortunately seldom seen as an even row but more often as two sets of three, one set being in line either with first slip's head or silly mid-on's feet. Twelfth man trotted out with a jug of glucose in time to avert the collapse of the bowler and the ruin of his analysis. Neither umpire could remember any rules applicable to such a complication, but after a lengthy argument it was decided to count the four balls as an over and resume from the other end. Two wickets promptly fell, one being that of the visiting captain, who complained bitterly and not unjustifiably about the mechanism of his defeat.

Our manic was wicket-keeper and had two habits which doubtless caused the late Dr. W. G. Grace much subterranean revolution. First, he never stopped talking throughout the match and many a batsman, through trying to follow the flight of ideas with his ears, failed to follow the flight of the ball with his eyes. Secondly, he appealed deafeningly for any ball that so much as touched a batsman, be it on belly, breast, or brow notwithstanding. Unnerving at the best of times, this technique was particularly successful now because our umpire at the other end was a passive homosexual midway through a course of electrical convulsion therapy. This masochistic little chap would rather die than hurt other people's feelings by disagreeing with them, and he raised his finger in dismissal if our manic so much as looked hopeful. Brisk rebuke and brief psychotherapy had to be administered to these respective gentlemen before the arrival of the next batsman. He, however, had been much unsettled before even reaching the crease, for as he passed cover-point that fieldsman whispered with intensity, "I know what you're thinking about me but you're wrong!" Consequently this batsman was too self-conscious to do anything but hit the first ball straight back into the bowler's hands.

This was the last incident for quite a time and things went almost normally till our turn came to bat. They had a very useful spin bowler, who was also, unfortunately, a very dusky West Indian. Number four in our batting list had embarked on his paranoid schizophrenia

Digitized by Google

in West Africa with beliefs, supposedly false, that the darkies were depriving him of his virility by means of witchcraft. Now he complained that this Sambo was making meaningful faces at him in the course of his run-up. He also suspected that the ball had been rendered radioactive—certainly a novel, if improbable, adjunct to any bowler's armoury.

Logic did not prevail: number four stalked off the field and was entered in the score book, after another conference, as "retired hurt." This apt suggestion came from the opposing captain, who now seemed, much to our relief, to be entering into the spirit of the thing. Even so, it was perhaps as well we lost by 40 runs.

* * *

When my friend the physiologist proposed that we should go and watch the Olympic weight-lifting, I responded with negative enthusiasm. Why, when the world is so full of a number of things, why choose weight-lifting? But his ardent pursuit of any and every phenomenon of the physical universe is infectious as well as enviable. So in due course we took our seats, armed cap-à-pie—he with an enormous pair of binoculars and I with a pencil and the back of my ticket (for working out averages and standard deviations and all that: la science, toujours la science!).

Why are negroes so successful in athletics? The physiologist speculated on the advantages of a less excessively developed cortical control, and referred me to the shorter reaction times that have been observed with left-hand responses; presumably the cortex leaves the left hand to its own devices a little more than the right. As he said, you can have a manager or a second to do any preliminary planning that may be necessary; when the gong sounds it is best to be a complete blank from the basal ganglia upwards, to avoid any "psychopathology of everyday life." Perhaps it would have been possible to estimate the I.Q. of the competitors from their idiosyncrasies when they mounted the stage. One man invariably plodded backwards and forwards across the back of the stage several times, then marched up to the bar, grasped it—and then straightened up again. The suspense was terrible. Another always stood over the bar for 38 seconds (average), apparently in deepest thought (possibly self-hypnotism). Others adjusted the bar to exact parallelism with the front of the stage. None took less than 3 seconds over these preliminaries, the mean being 10·65 seconds. My ticket was too small for me to work out the standard deviation, but I don't suppose you care. Also—I nearly forgot—weights were lifted, phenomenal weights. Given the necessary muscle, the great thing here is coördination, particularly in the way of balance; it doesn't do to topple when you are supporting the equivalent of two 12-stone men. Many resounding thuds testified to this. Finally, I must spare a word for the three judges, who gave their decisions, often on subtle technical points, almost before the bar had reached the floor—not always to the satisfaction of the spectators, who were not diffident in expressing their own opinions. Altogether, a good time was had by all, including the two scientists.

* * *

Most doctors seem to be feeling frustrated over the question of new cars just now; but few can have experienced the refinements of torture suffered by myself, a poor struggling assistant in the suburbs of Coventry. As I bounce (literally) along the streets, most of which appear still to be suffering from the effects of the blitz, while my poor 1935 Morris "8" rattles with loose bodies in every joint, agony piles on agony as a succession of new Jaguars rolls by on test (I did experience a certain thrill at seeing one of the breed speeding along a nearby country road with test-plates and left-hand drive). Humbers, Hillmans, Standards, and Triumphs, all shining new, seem to be posted at strategic points along every road expressly to make my torture worse. At really bad moments I go along and park outside the Riley works and gaze wistfully at the new models in the yard. I have one slight consolation. By the time I can afford a new car the shining beauties I see today may all be going second-hand for a mere twenty pounds or so.

Letters to the Editor

INTEGRATION OF ANATOMY AND PHYSIOLOGY

SIR,—A year ago you published a letter[1] recording the results of the first examination taken in the integrated curriculum for anatomy and physiology which Birmingham University instituted in 1946. This preliminary information was submitted in response to a request from one of your correspondents, and we undertook to add to it, as we can now do, after the second part of the course had been completed. As some time has elapsed since our last note on the subject, it would be advisable in the first place to outline the main innovations of the Birmingham curriculum. They are:

1. To combine the anatomical and physiological approach in every course of lectures, and to avoid separate courses in the two "subjects."
2. By divesting the subject of much unwieldy, and probably unnecessary, detail, to confine dissecting-room anatomy to three instead of five terms.
3. To devote the anatomical teaching of the fourth and fifth terms to surface and radiographic anatomy and to neurology.
4. To divide the 2nd M.B. examination into a first part, dealing with topographical anatomy and histology, taken at the end of the third term, and a second part, dealing mainly with physiology and functional anatomy.

In October, 1946, the first integrated course was begun by 83 medical students. In the following June 81 took the part 1 examination and 58 (about 70%) passed; 22 out of the 23 who failed, and one of 2 students who had been absent from the course because of illness, prepared for the referred part 1 examination in September, 1947, when 21 presented themselves for examination and 14 were passed. The 7 who failed were asked to withdraw from the school.

The 72 students who had completed the part 1 examination took the courses of the fourth and fifth terms of the curriculum, which, in addition to the usual laboratory classes in physiology and biochemistry, included practical classes in neurology, surface anatomy, and radiology. All sat the 2nd M.B. part 2 examination in March of this year. The examination comprised two written papers, one of which included three questions of a morphological nature. Practical examinations were held in biochemistry, in experimental physiology, and in anatomy. The anatomy examination, which was in the form of a viva voce, not only covered those aspects of anatomy that had been actively taught in the fourth and fifth terms, but also attempted to discover how much knowledge of topographical anatomy had been retained by the students. The standard of the whole part 2 examination was at least as high as the usual 2nd M.B. examination. All but 10 of the 72 candidates satisfied the examiners. The 10 who failed were allowed to sit a referred part 2 examination in June, when all but 2 passed.

We were agreeably surprised to discover a high standard of retention of topographical knowledge, and, so far as the anatomical aspect of the integrated course is concerned, we are satisfied that the students who have now completed the course have at least as good a knowledge of topographical anatomy as is usually demanded from 2nd M.B. candidates. We are also confident that their familiarity with neurology is greater than is usual in 2nd M.B. students.

The whole course has permitted two separate evaluations of all students under full examination conditions, and in the case of those who failed either the part 1 or part 2 examination (or both) three or four. It is possible, therefore, to derive certain further information about performance and about the likelihood that a student's showing in the part 1 examination is an indication of his probable results in part 2. All 42 candidates who achieved a mark of 55% and over in part 1 passed in their first attempt at part 2. Of 16 who obtained between 50% and 54% in part 1, 12 passed in their first attempt at part 2. The 4 who failed sat the part 2 referred examination; 3 satisfied the

1. Boyd, J. D., Smout, C. F. V., Zuckerman, S. *Lancet*, 1947, II, 150.

Digitized by Google

examiners, and the 4th (who was a "borderline pass" in the part 1 examination) has now withdrawn from the medical school.

All students who failed in their first attempt at the part 1 examination and who received between 45% and 49% of the marks passed the part 1 referred examination, but subsequently had difficulty with the part 2 examination. Those who failed part 2 on their first attempts succeeded, however, on the second. All our eventual failures came from the group who did not get 45% in their first attempt at part I. Those of this group who ultimately succeeded in passing part 2 did so by a very narrow margin.

Of the original 83 students who commenced the integrated curriculum in anatomy and physiology, 70 have therefore moved on to the fourth year of the medical course; 9 were referred in examinations, 2 have withdrawn of their own accord, and 2, who were away because of illness, have fallen back a year.

The high correlation in the showing of students in part 1 of the examination, which is mainly topographical in emphasis, with that in part 2, which is mainly physiological, is interesting. We should like to think that it is, at least in part, attributable to the close integration of anatomical and physiological teaching throughout the course.

Department of Anatomy, London Hospital Medical School. — J. D. BOYD

Department of Physiology, Leeds School of Medicine. — A. HEMINGWAY

External Examiners.

Department of Physiology, Birmingham Medical School. — H. P. GILDING

Department of Anatomy, Birmingham Medical School. — C. F. V. SMOUT, S. ZUCKERMAN

Internal Examiners.

LATENT TETANY CAUSED BY BAL

SIR,—The article by Dr. Russell and colleagues (July 31) calls for some comment as the authors' conclusion that "all the symptoms of toxicity from BAL are capable of explanation as latent tetany" is hardly substantiated by the reported facts. The symptoms of latent tetany are not reliable diagnostic criteria. They are variable and may simulate a number of other conditions such as anxiety state, asthma, hysteria, and epilepsy. Also, if a patient in latent tetany develops cramps he almost invariably develops some degree of carpopedal spasm, and this was not specifically mentioned as having been seen by the authors. Furthermore, the list of symptoms noted with BAL intoxication includes items which are very rare in latent tetany—e.g., vomiting, and a burning sensation or pain in the eyes, nose, mouth, and throat. Tingling or numbness is the more typical symptom of latent tetany. Severe abdominal pain does not occur except in gross tetany with definite carpopedal spasm.

The fact that Trousseau's sign was negative except in one instance is also contrary to what one would expect in latent tetany. Indeed, the single positive response out of thirteen subjects is what might be found with any group of young adults who are physically upset by the injection and collection of blood. It is also unwise to base a diagnosis of latent tetany on Chvostek's sign; in 72% of hypocalcæmic adults it was negative,[1] while Graham and Andersen [2] have condemned it as a phenomenon unrelated to tetany. From my recent experience (in the press) it seems reasonably reliable in the acute tetanies such as Dr. Russell and colleagues were studying. It must be accepted with precautions, and the degree of response should be recorded in some accepted classification such as that of Frankl-Hochwart. Lastly, the study of electrical excitability is not in agreement with the diagnosis of latent tetany.

These criticisms are offered with the feeling that the hypothesis is not established and yet is not necessarily false. Indeed it should be easy to decide the issue by giving BAL plus constant intravenous calcium gluconate; and also by producing experimental hyperventilation tetany [3] in the subjects later and comparing the symptoms with those of BAL intoxication. If the existence of tetany with BAL intoxication is established the cause must be sought in the usual places first. The patient whose case was recorded by Dr. Russell complained of vomiting and profuse sweating, and may well have been hyperventilated. The single estimation of alkali reserve done some days after the last BAL injection does not disprove the possibility of alkalosis tetany.

Dublin. D. K. O'DONOVAN.

1. O'Donovan, D. K. *Irish J. med. Sci.* 1945, p. 146.
2. Graham, S. G., Andersen, J. H. *Lancet*, 1924, i, 1307.
3. O'Donovan, D. K. *Irish J. med. Sci.* 1943, p. 564.

SMALLER AND BETTER PRACTICES

SIR,—Your leading article of Aug. 14 is very much to the point. General practice is in danger of being swamped by a tidal wave of patients requiring attention. Many items are trivial and can be attended to by a good secretary with some first-aid training. There are the requests for corsets, glasses, milk, drug repeats, and miscellaneous certificates; there are continuation dressings and routine injections. Perhaps a short account of a partnership in an urban and rural district which is organised to produce the maximum medical efficiency and to avoid all non-medical and trivial tasks would help others confronted by new threats to their standards of medicine.

My partner and I have about 4000 patients between us. We cover an area of 60 square miles and we motor about 1200 miles a month on our rounds. We work 12–14 hours daily and allow ourselves one half-day a week and two Sundays in a month free of calls or other duties. Our secretary is busy from 10 A.M. until 7 or 8 P.M. We hold surgeries three times daily at the urban centre and twice weekly at two rural centres. But these surgeries are performed by one of us only, in a fixed and equal rota. In this way all our patients are assured of seeing either of us at one or more surgeries every day at the centre and once weekly in the two rural surgeries. They all know which of us will be on duty at any particular surgery, and if in doubt can inquire from our secretary. This member of the team is most essential and acts as a screen to shield us from trivial tasks and wasted time.

Our nearest laboratory is 15 miles away. X-ray facilities and the county hospital are 30 miles away. There are no medical consultants of the first degree nearer than 70 miles away. Consequently we try to be comprehensive and only send cases away for very complicated investigations and for surgical treatment. In order to undertake proper medical diagnosis we find the following equipment is necessary:

1. A microscope and bacteriological stains for blood-smears, sputum tests, and centrifuged deposits of urine.
2. Apparatus for accurate hæmoglobin estimations (Sahli's for domiciliary use and Haldane's for surgery use); hæmatocytometer tubes for red and white cell counts; special stains for reticulocyte counts.
3. A Westergren blood-sedimentation tube.
4. Gerrard's ureometer for urea-clearance and urea-concentration tests of renal function.
5. An X-ray apparatus with a fluorescent screen for assisting in the diagnosis of heart, lung, and gastric disease, for the treatment of fractures, and for the assessment of injuries and diseases of joints. We have found many new cases of tuberculosis in this way, and have been able to reassure many patients of the absence of pulmonary or cardiac disease. All cases presenting doubtful X-ray appearances are naturally referred to an appropriate specialist.

A good secretary can take routine X-ray films and develop them. She can do blood-counts and test urines. She controls the internal telephone exchange and deals with all incoming messages at her discretion, passing some on to our private residences or surgery, or simply taking action without bothering us. In this capacity she contacts specialists, house-surgeons, and colleagues by telephone, and saves us hours of waiting on the line.

We use a consulting-room and a separate smaller examination-room, so that any patient requiring a complete examination can be by-passed to the latter without interrupting the surgery circulation. The consulting-room also has a completely screened-off couch for full examinations. By these methods two patients can be seen at once in little more time than it takes to chat about the weather and the news to one patient dealt with by the "bottle-of-medicine"

Digitized by Google

technique. The examination-room is invaluable for fluorescent screening, ophthalmoscopy, antrum illumination, and any dark-room technique. It is also used for minor dressings, routine injections, and antenatal supervision.

We are both fully occupied with our patients' health and welfare, and we try to give them comprehensive medical supervision. We are doubtful if we can achieve a sufficient income under the N.H.S. for such an expensive outlay and service. We are faced with the possibility of having to reduce our standards of practice unless the Government are willing to recognise the financial strangulation of smaller practices. Yet better medicine can only be done with a smaller list.

Grange-over-Sands. P. D. MULKERN.

SIR,—Having read your recent leading article (Aug. 14) on the maintenance and improvement of the standard of general medical practice, may I point out another major aspect of the N.H.S. which militates against this? Every improvement in facilities—every instrument or apparatus that is now acquired by a general practitioner—is a financial loss. He cannot charge his patients even a small fee to cover the actual cost of it. If he does not provide any improvements his income will remain much the same. There appears no incentive, except the doctor's pride in his work, to provide more than routine treatment. In fact financial loss loads the balance against any display of initiative.

Burley, Hants. P. R. G. HOWARD.

ARTIFICIAL INSEMINATION

SIR,—At the risk of appearing unduly sensitive, I am requesting you to allow me to reply to certain criticisms in the report of the Archbishop of Canterbury's Commission on Artificial Insemination [1] bearing upon a memorandum issued by the Medical Defence Union.

The union's memorandum did not purport to be an exhaustive study of the subject from all angles, and this the union had neither the facilities nor the intention to undertake. It was written, as the headnote states, solely with a view to the protection of practitioners who engage in the practice of artificial insemination. In these circumstances the criticism that the memorandum is "superficial" is entirely unjustified.

It is, moreover, stated that the memorandum is "grossly misleading," but no indication is given of the reason for such strong language. The chapter of the report dealing with the legal aspects of artificial insemination fails to reveal any basis for the criticism, unless it be that the writers have confusedly attributed to the union the authorship of an article in a medical journal [2] or assumed that the union shared the views expressed in that article. Should this be so, it is appropriate now to repudiate on the council's behalf both the authorship of the article, and agreement with the views therein expressed.

It is conceded, of course, that the union's memorandum did not make reference to the difficulty that will arise over the registration of the birth of an infant resulting from artificial-insemination donation, since registration is not a matter with which the practitioner is normally concerned. The difficulty is a very real one, and to it further consideration will be given by my council in the future; for this constructive criticism we are grateful.

It is regrettable that the authors of the chapter in question should have thought it proper to publish strong condemnation of the views expressed by the union in a matter of complexity and public importance without first giving to the union some indication of their intention and an opportunity of expounding its views. The very eminence of the authors in their own field promotes an expectation that the usual courtesies would have been observed.

It should further be noted that permission to publish the union's memorandum as an appendix to the report was only sought when the report itself was in galley proof and at a time when the urgency of publishing the report precluded the union from properly considering whether the memorandum—prepared, as it was, with a different object in view—was suitable for such publication. I add with regret that neither then nor at any other time was there any communication to the union that the memorandum was or would be made the subject of criticism.

Except for the single matter mentioned above, there appears at present no need for the union to modify in any way the advice to its members set out in its memorandum.

49, Bedford Square, London, W.C.1. ROBERT FORBES
Secretary, Medical Defence Union.

1. See *Lancet*, Aug. 21, p. 298.
2. Barton, M., Walker, K., Wiesner, B. P. *Brit. med. J.* 1945, i, 40.

BEDS FOR PULMONARY TUBERCULOSIS

SIR,—In his letter of Aug. 7, Dr. Tattersall discusses the problem of making 15–25 beds serve the needs of a population of 110,000 with a tuberculosis death-rate of 60–70 per 100,000. It would not be surprising if in such a situation his motives were to become somewhat mixed. Should he regard tuberculosis as an individual problem? In this case every patient, regardless of the extent of his disease on diagnosis, would be equally entitled to a treatment bed. Should his chief concern be the potential infectivity of his patient? In this case segregation and even the most risky form of treatment might be justifiable. Should he be concerned with the wider social problems affecting the tuberculous family? In this case the middle-aged breadwinner with relatively extensive disease should have priority over the young daughter with the minimal lesion. Some light may be thrown on Dr. Tattersall's dilemma by reference to Wicksteed on "Administration of Resources and Choice between Alternatives." [1] At the present time his judgment is perhaps influenced by his belief in the efficacy of quick collapse therapy, and he claims that he has rendered 30% of his infectious cases "safe" by these means, though "their ultimate fate is undetermined."

The correspondence which has followed Dr. Bentley's article illustrates the extremities of medical improvisation to which we are driven by the inadequacy of the bed accommodation for the tuberculous. Surely we should abandon the pretence that a brief admission to a bed to make some adjustment in the respiratory mechanism can exert a lasting influence on a disease with such a complicated ætiology as pulmonary tuberculosis. The patient himself requires long and careful handling, and the "crash A.P." for the early lesion is more often than not a disastrous measure. The introduction of streptomycin will further complicate therapy, and will call for an even nicer judgment in timing surgical intervention.

Some facts in the situation cannot be disputed: pulmonary tuberculosis is the greatest destroyer of young adult life; it presents an immense social problem, but given time and opportunity treatment can be most efficacious. Can these things be said of many of the conditions which secure admission to the medical and surgical wards of general hospitals? It is surely true to say that on the medical wards of a general hospital the average age is nearer 60 than 20, and the patients often suffer from intractable and untreatable diseases. Yet the main nursing effort of the country is concentrated on this relatively unpromising material, to the disadvantage of urgent and treatable cases of young adult phthisis.

It is an interesting thought that if each of the general hospitals in this region were to second one nurse every three months, for special duties and training, to the chest hospital from which this letter is written, it would be possible to open at once the beds which are now closed through lack of nursing staff. The present wait for admission is nine months.

County Hospital, Harefield, Middlesex. L. E. HOUGHTON.

SIR,—The letters of Dr. Tattersall (Aug. 7) and Dr. Stradling (Aug. 21) both put forward useful suggestions for overcoming, at least partially, the difficulties in finding suitable accommodation for the tuberculous patient. Particularly valuable is Dr. Stradling's suggestion for the reallocation of hospital beds in general, so that more can be devoted to the treatment of the young tuberculous adult.

Some of his views, however, are more debatable—for instance, it seems doubtful whether the beds now used for the treatment of the chronic case could be used

1. Wicksteed, P. H. Common Sense of Political Economy. London.

Digitized by Google

for the treatment of a number of young persons with early disease "in succession." It is just these early cases which respond well to a strict and prolonged régime of bed rest, with or without associated collapse therapy. It is apparent from the average type of case admitted to hospital or sanatorium that not all physicians agree with Dr. Stradling's selection of cases; in fact, at times one wonders if the available beds are not considered by some to be for the use of the homeless and incurable. We do not think the bed position would be greatly improved by giving the chest-clinic physician "direct control" of all beds. We think the answer lies in closer coöperation between the hospital and sanatorium physician on the one hand, and the clinic physician on the other. Let the first have his outpatient department where he can see old and new cases, diagnose, treat, and follow them up, and let the clinic physician have beds in hospitals. It is impossible to expect the clinic physician to undertake the care of more beds and also act as consultant and specialist for a population of a quarter of a million or more, often spread over wide areas; our Scandinavian colleagues usually serve an area containing a population of about 60,000, and no treatment is undertaken by the clinic. By handing over some of the outpatient work to the sanatorium team, the clinic physician could ease the burden upon himself, although a much greater number of physicians will be needed to work an efficient service.

There is no doubt that the centrally administered waiting-list causes too much separation between the clinic physician and chest hospital. Much could be done to improve this position and make coöperation more practicable if chest hospitals were affiliated to nearby clinics. Cases could then be referred direct to the hospital covering the area, and the more direct contact would offer a chance of real coöperation between chest hospital and chest clinic.

Is it not time that cases requiring major thoracic surgery came under the personal preoperative and postoperative supervision of a surgical team with its own beds and waiting-list? The clinic and sanatorium physician would each consult freely with the surgeon, who would then decide the relative urgency and optimum time for operation in each case. Few surgeons would disagree that it would be wise to have a physician of experience attached to each surgical team for day-to-day consultations. We feel certain that in this way better use would be made of beds, and a better service afforded to our patients.

Finally, it should be obvious that any suggestions for overcoming the present lack of beds by lowering the standard of nursing and medical treatment, are to be deprecated as a long-term policy. The remedy lies ultimately in taking whatever steps are necessary to remedy the nursing shortage.

B. J. DOUGLAS SMITH
C. J. STEWART
W. E. SNELL.

Colindale Hospital,
London, N.W.9.

SIR,—The magnitude of the problem created by the shortage of beds for patients with pulmonary tuberculosis is indicated by the frequency with which this question is discussed in your journal. Waiting-lists are as long as ever. Until more beds are available, the chest physician must use the beds at his disposal so that as many patients as possible receive treatment in the shortest possible time. One of the means to this end is a drastic reduction of stay at the sanatorium before and after collapse therapy, careful consideration having been given to all the relevant factors, including home conditions.

Collapse treatment in the patient's home can play an important part in shortening the waiting-list, as has already been observed.[1] It can be started in the home not only in cases with minimal disease but also, without undue risk, where the disease is moderately advanced, whether unilateral or bilateral, especially when the patient's reserves seem nearly exhausted. A few weeks or months of preliminary rest in bed will point the way to be followed in treatment. The patient with bilateral disease still suitable for collapse therapy can have at least one pneumothorax successfully established while waiting for admission; once admitted, if in need of major surgery for his other lung, he may need only a short spell for detailed investigation before he is ready for operation.

Perhaps the greatest difficulty in carrying out domiciliary collapse therapy lies in picking the right type of patient. So far, I have done about 30 inductions in patients' homes. Among the criteria I consider of major importance are: the X-ray appearance, the patient's attitude to the prospect of protracted rest in bed, his temperament, and finally the home conditions. The X-ray appearance should be such that the success of collapse therapy appears probable; and before induction the patient must have stayed in bed for at least 1–2 months. To check on this, I usually visit the house a few times without previous warning; generally speaking, the patient must be a "collaborator." At his home the patient should have at least somebody in the house to prepare his meals and be at hand. Sympathetic guidance may often help to create more tolerable conditions in the house.

The success of any treatment depends materially on the patient's morale, especially when treatment is lengthy. Now that the value of collapse therapy is generally known, it is difficult to persuade a patient that all he needs is rest in bed at home for 6 months or longer. Treated in this way, his morale may have vanished long before he is admitted to sanatorium—and with it his prospect of a favourable prognosis. We are all agreed that the ideal place for this therapy is the sanatorium, but while reaching for the desirable we must not by-pass the attainable. The acceptance of Dr. Stradling's suggestion regarding continuity of treatment would foster domiciliary collapse treatment.

City of Leeds Health Clinic. HERMANN GRUNWALD.

1. Maclean, A., Gemmill, J. S. *Lancet*, 1948. i. 173. Pritchard, E. K. *Ibid*, p. 302. Stradling, P. *Ibid*, Aug. 21, p. 311.

MEDICAL USES OF POLYTHENE

SIR,—Let me congratulate Dr. Farquhar and Dr. Lewis (Aug. 14) on their description of a technique which is, as they claim, a definite advance in intravenous therapy. Ureteric catheters have, of course, been used in somewhat similar fashion for many years with varying degrees of success. I would be interested to know what means they adopted, apart from splintage of the proximal flexures, to prevent the normal posture of flexion of the infant, particularly in the arms, stopping the flow of fluids by kinking the veins.

However, before Bateman's and similar cannulæ are discarded one might point out that very successful intravenous therapy is possible with them; in the gastro-enteritis unit at this hospital many "cut-downs" have lasted for seven days or more with minimal phlebitis, and one, regarded as somewhat of a record, ran for fourteen days with very little venous reaction.

That the elimination of trauma to the vein, apart from the initial insertion, is important is well shown by the readiness with which a phlebitis will occur in a restless infant, as distinct from the placid or flaccid one. Other factors are of considerable import, such as the substances used for transfusion or infusion and the avoidance of unnecessary interference and infection; but I have always been impressed by the need for adequate and secure splintage, and for sedation of the very restless infant when rigid cannulæ are used. The flexible catheter reduces this factor to a minimum.

My main object, however, is to plead for a more general adoption of a technique which appears to be the routine in most trans-Atlantic units and in some Continental ones—that of direct venepuncture. The success with which this method is practised depends mainly on the environment and the enthusiasm with which it is fostered. Following the advent of a Canadian lady for a tour of duty on our gastro-enteritis unit, for some months over 50% of all intravenous infusions were done by this technique. As an example, one infant, the severity of whose illness necessitated continuous intravenous therapy for 28 days, left hospital with only one "cut-down" scar. One of these "stab" drips has run for nine days, at an average rate of a litre daily, taking various fluids including 5% glucose, Darrow's solution, blood, and plasma. For the actual venepuncture, selected hypodermic or small intramuscular needles can be used;

Digitized by Google

short-bevel needles are better retained in the vein but are often difficult to insert. The Frankis Evans type of double needle has particular advantages. The veins of election are those of the dorsum of the hand and foot, but the radial, antecubital, and long saphenous veins can occasionally be used in an infant without much adipose tissue. Adiposity is the biggest obstacle to successful venepuncture as the vein cannot then be readily seen or palpated. The largest needle that can successfully be inserted in the vein is naturally the one of choice. The method of securing the needle and of splintage are of great importance. The main advantages of this technique are that the vein more readily re-canalises; there is much less phlebitis and periphlebitis; wound infection cannot occur since there is only a needle puncture; no scar results; and veins which may be of vital value to an infant can be spared.

Finally, I cannot agree with the writer of the section on intravenous therapy in a recent pædiatric textbook that "it is practically always necessary to cut down on the vein in children younger than five years." Surely we should make it an accepted principle in our pædiatric units that direct venepuncture is the method of choice in every child unless there are definite reasons to the contrary.

Queen Elizabeth Hospital for Children, London, E.2. B. McNICHOLL.

SIR,—With reference to the most interesting article by Dr. Farquhar and Dr. Lewis, for some time I have used polythene tubing in the treatment of varicose veins, inserting it up the saphenous vein after doing an "ankle tie." It has just the right resistance and it is far more practical and very much cheaper than ureteric catheters, which require special sterilisation and deteriorate rapidly after being used once or twice.

London, W.1. R. ROWDEN FOOTE.

PROFESSIONAL SECRECY AND VENEREAL DISEASE

SIR,—I write in support of Sir Ernest Graham-Little and Miss Hardwick (Aug. 14). I am confident that the promise of secrecy, contained in the original V.D. scheme, encouraged patients to attend a clinic and—of equal importance—to continue under treatment. The original scheme, which resulted from Sir Malcolm Morris's energetic campaign, produced a steady decrease in the incidence of syphilis throughout the inter-war years; the L.C.C. returns record 8118 new cases in 1921 and only 2864 in 1938. It would be lamentable if such progress should be jeopardised by the new decree. Nor should we forget the honourable tradition of our profession, not to divulge what we see and hear in connexion with our professional practice.

London, W.1. HENRY MACCORMAC.

SALARIES IN GOVERNMENT SERVICE

SIR,—The Spens report on the remuneration of specialists and other whole-time hospital medical officers suggested that clinical work should be remunerated more fairly than in the past when higher salaries meant diversion to administrative work.

The Ministry of Pensions has reviewed the salaries of hospital medical officers and has just notified them individually of the new scales. The notification received by me does not indicate whether any increments will be allowed in future years. Nor has any provision been made for superannuation, for the Ministry stays out of the National Health Service and is not bound to accept the principles of the Spens report.

I have been employed for some years at the maximum rate of £550 per annum (plus £100 living-out allowance and £90 consolidation allowance, making a total of £740). I have reached this by annual increments (which had to be requested) from the starting salary of £350, and was informed on application in recent years that the Ministry did "not usually pay more." My new salary has been consolidated at £890 per annum.

This information may enable hospital medical officers not employed by the Ministry of Pensions to obtain some idea of their new salaries.

"TEMPORARY" MEDICAL OFFICER.

THE ALCOHOLIC

SIR,—It was instructive to read how your contributor (Aug. 7) broke away from alcohol with the aid of Alcoholics Anonymous. Yet, few addicts are capable of performing such a feat unless medicine has paved the way; it is in aftercare that Alcoholics Anonymous excel. This is no mean division of labour: patients stand or fall by the aftercare they receive, and doctors cannot provide it. What doctors can provide in the way of treatment may be seen from Dr. J. P. Henderson's [1] personal account of alcoholic craving; a more fitting complement to your contributor's story would be hard to find.

Falmouth. H. PULLAR-STRECKER.

M.R.C.P. EXAMINATION

SIR,—The opinion is indeed widely held that the M.R.C.P. is no longer a clinical examination of high standing. This viewpoint would appear to be justified for two reasons: (1) the results of the examination have become notoriously unpredictable, and (2) no candidate is required to have done any clinical work. The only regulations with which a candidate must comply are some curiously applied rules relating to the primary qualification. The large number of prospective consulting physicians obviously makes the introduction of detailed regulations essential.

The success of even a small proportion of recently qualified doctors who cannot possibly have acquired the necessary experience certainly discredits the examination. The numbers who take it "on spec." and find themselves on the pass list must be embarrassingly high.

Since the era of the general physician is passing and nearly every would-be consultant ultimately specialises in one or other of the branches of medicine, we wonder whether the London college has considered adopting a plan such as that of the Edinburgh membership.

For this examination a candidate must be qualified for two years and in addition to "the principles and practice of medicine" must offer a special "department of medicine . . . in which a high standard of proficiency is expected." Each of the two sections of the examination consists of (1) papers; (2) a series of short cases in the form of a ward-round and a long case for written commentary, with a "clinical-oral on diagnostic methods" such as X rays, cardiographs, histological slides, clinical specimens, &c.; and (3) an oral examination.

A test such as this has several advantages. It is long and therefore can be thorough. It greatly reduces the element of chance. The examination in the high-proficiency subject is especially attractive to those young enthusiasts who are beginning to pursue their life's real interests. One modification, however, which would enhance further the status of the examination would be the extension of the required period after qualification to three or more years, part or all of which should be spent in recognised appointments.

M.R.C.P. LOND.
M.R.C.P.E.

DEATH WHILE BATHING

SIR,—There has often been uncertainty about the real cause of deaths whilst bathing. Those who have recovered from an attack which apparently would have caused their death had it occurred while swimming in deep water can help to throw light on the subject, as Dr. Alexander [2] has done. Zum Busch's [3] account of his own experiences suggests that a kind of giant-urticaria and faintness following sudden immersion in cold water may both be explained in the same way, the giant-urticaria being due to the release of a histamine-like substance in the skin and subcutaneous tissue, which, if too much gets into the general circulation, may cause fainting.[4] A popular summing-up of the histamine part of the subject is given by Langdon-Brown [5]:

> "Every known protein contains . . . histidine. Break off a single CO_2 molecule from this histidine, and it becomes

1. *Brit. J. Inebr.* 1944, **42**, 44.
2. Alexander, G. L. *Lancet*, Aug. 21, p. 312.
3. Zum Busch, J. P. *Dtsch. med. Wschr.* 1933, **59**, 15.
4. Horton, B. T., Brown, G. E. *Amer. J. med. Sci.* 1929, **178**, 191.
5. Langdon-Brown, W. *Camb. Univ. med. Soc. Mag.* 1932, **10**, 38.

Digitized by Google

a powerfully toxic substance, histamine. This substance when liberated from the tissue cells can produce all the phenomena of allergy. The chemical basis of allergy is therefore simple . . . but the factors which lead to the liberation of this substance are almost as varied as life itself. Histamine was originally isolated by Barger and Dale from ergot in 1910, and then from the intestines. If it is applied to the human skin, it promptly raises an urticarial wheal; if injected intravenously into animals, it produces a condition like anaphylactic shock. . . . The problem is, how does a substance which is toxic to everybody become liberated only in the tissues of certain people, in answer to stimuli which are quite harmless to everyone else."

Zum Busch would probably have died had he been in deep water at the time of a severe attack. There is a good deal of scattered literature on similar severe reactions following sudden immersion in cold water. But Goebel [6] relates his personal experience, when he was nearly drowned while swimming in water which was not cold, on a warm summer day. The accident occurred, however, soon after the midday meal, and may have been connected with his stomach being full.

London, W.1. F. PARKES WEBER.

APPOINTMENTS AND POLITICAL ACTIVITIES

SIR,—In the official document "Appointments as Member of a Medical Board Panel under the National Insurance (Industrial Injuries) Act, 1946" the following sentence occurs at para. 5: "In view of the judicial nature of the statutory functions assigned to medical boards under the Act, members are asked to notify the regional medical officer of the Ministry if they play, or intend to play, a prominent part in politics." I gather that they will then be called on to resign their appointments.

I submit that the survival of democracy depends on the political activity of its intelligent members.

BELSEN.

MEDICAL RECORDS

SIR,—I should like to support "Medical Secretary's" plea (Aug. 14) for special training for those wishing to become medical stenographers. As medical superintendent of a hospital, I have had to train four shorthand-typists in the last seven years. I personally dictate all the discharge reports and outpatient reports, and the tremendous amount of time wasted in spelling out medical terms, quite apart from the resultant fraying of tempers, has to be experienced to be believed.

My present secretary fully agrees with me that there should be some course of instruction for would-be medical stenographers. When she took up her appointment with me she had had considerable experience in lay stenography in the local council offices, and it was galling to her to find her speed reduced to a mere trickle owing to the necessity of getting words spelt, or of looking them up in the medical dictionary.

I have no personal knowledge of the "notorious meanness" of doctors when it comes to paying their secretaries, as I have worked in hospitals all my qualified life; but I do know that local authorities are slow to recognise financially the extra application required of medical stenographers. My secretary receives no more pay than girls with the same number of years' experience in the central office, where the work is purely lay; and yet she has to carry in her head details of the spelling of hundreds of abstruse medical terms.

I have lately begun to train a new outpatient clerk, and am feeling to the full the difference between one trained in the use of medical terminology and one who is not; whereas I am able to dictate my inpatient discharge reports with an average amount of pleasure, I approach the dictation of my outpatient reports with a feeling of misgiving which very shortly becomes exasperation.

I feel sure that if only they would take the trouble to write to you, most doctors would endorse the need for suitably qualified stenographers.

MEDICAL SUPERINTENDENT.

6. Goebel, O. *Dtsch. med. Wschr.* 1934, 60, 982.

Obituary

JOHN KAY JAMIESON

M.B. EDIN., LL.D. LEEDS, M.A., CH.M. DUBL.

Prof. J. K. Jamieson, who successively held the chair of anatomy in the University of Leeds and at Trinity College, Dublin, died on Aug. 20, at the age of 75.

He was born in Shetland, the fourth son of Robert Jamieson of Sandness; and E. B. Jamieson, the Edinburgh anatomist, is one of his brothers. From Madras School, St. Andrews, he went to the University of Edinburgh, where he qualified M.B. in 1894. After holding a demonstratorship in anatomy at Surgeons' Hall in Edinburgh he took up the same post in the University of Leeds under Wardrop Griffith, whom he succeeded in the chair in 1910. During the 1914–18 war, as deputy dean of the faculty of medicine, he proved himself as an administrator and the twenty years of his deanship which followed was a time of notable expansion for the faculty especially in the departments of pathology and physiology. From 1928 to 1936 he was also a member of the General Medical Council, and he acted as examiner for the universities of Edinburgh, Aberdeen, Liverpool, Manchester, Sheffield, Bristol, Dublin, and Belfast.

In 1936, when he had almost reached retiring age, Jamieson was appointed to the chair of anatomy at Trinity College. The intention was that he should retire in 1943 at the age of 70, but conditions that year were unfavourable for the appointment of a successor, so, despite failing strength, shortage of staff, and scarcity of fuel he carried on until last summer. Even then he was not immediately granted a respite, for his successor was unable, through illness, to take up his duties in October and Jamieson continued as acting professor until last December.

Of these years in Dublin J. W. B. writes: "It would not have been easy for anyone to maintain the reputation of a department of anatomy which had had at its head three such men as Alexander Macalister, D. J. Cunningham, and A. F. Dixon, but we asked Jamieson to do something more difficult than that—to break the tradition of the department. Dixon had maintained, unaltered, the Edinburgh tradition which he had inherited from Cunningham, a tradition which was excellent when medical students were given training in little except anatomy in preparation for their clinical work but a tradition which, in the opinion of the younger members of the staff of the school, had outlived its utility. So it fell to Jamieson to reduce the duration of formal teaching in anatomy from eight terms to five and to prove that, while a course of this length might be inadequate for the training of an anatomist, it was adequate for 99% of medical students. No young and inexperienced man and no-one whose reputation had not already been established could have succeeded as well as Jamieson did in this difficult task.

"Jamieson taught form and function and never failed to point out not only what was important in relation to clinical work but also why it was important. His lectures were always interesting and often entertaining, but it was in informal teaching in the dissecting-room that he excelled. There he might be found at any hour of the day, surrounded by a group of eager students each of whom he knew as an individual, dissecting and demonstrating, teaching the dull to use their brains and the clumsy their fingers. He inspired both respect and affection in his students: he never forgot a student whom he had taught and no student ever forgot him.

"The staff of Trinity College changes more slowly than that of most universities and does not readily

Digitized by Google

take to its heart a newcomer. But Jamieson, who had often acted as external examiner, was never regarded as a newcomer. His ability, his honesty of purpose, his sound common sense, his dependability, his wide knowledge of the classics and of English literature, all gained him the respect of his colleagues, but Jamieson gained something rarer than that—their affection. Those he met were first attracted by his little mannerisms, his learning so modestly displayed, his impish sense of humour, his kindness of heart, and, almost before they were aware of it, acquaintance had blossomed into friendship. When he gave—as he so generously did—friendship, he gave it for life. It was kept alive by meetings at long intervals and by his letters, which deserved leisure to read, not because his writing was crabbed or difficult, but because he packed so much into a couple of pages. During the war many widely scattered friends blessed him for the pleasure his letters gave. No doubt others will worthily take the place of Jamieson the great teacher of anatomy, but we cannot hope that anyone will fill the place left vacant in the life of the College by our friend Jimmy."

As a friend of thirty-seven years' standing J. C. B. adds: "Jamieson was a man whose arresting personality, instantly impressive to all on first contact, became a tradition in his own lifetime. When he appointed me his demonstrator, in the second year of his professorship at Leeds, I knew at once that I had acquired a friend as well as a chief; and experience amply proved that beneath a rather forbidding exterior, he imperfectly concealed an inherent kindliness that broke out in unexpected ways and places. Thus to many he had long been known by the revealingly affectionate name of 'Jamie.' With startling exceptions, he had little use for the conventions and conventional procedure. There was an impish quality about all his doings, sometimes disconcerting to his friends and colleagues; and it was a secret delight to him—sometimes not so secret—that he was thought by some to be Machiavellian in his methods. In an old letter, after recounting his reasons for accepting a post offered to him, he goes on: 'The first reason is childish though respectable: the other reasons savour of a life of intrigue. Now, I ask you, am I a crafty and devious person? This will put you up against it to frame an agreeable answer.' But, as a man of affairs, he certainly knew his business, and more often than not got his own way because it was the best way. He had the most penetrating judgment of men and their motives, and his advice, in private as well as in public matters, was always shrewd and solid.

"As a teacher of anatomy Jamieson's reputation was early established and stood high. His practical and characteristically fresh outlook on topography made his lectures and demonstrations occasions to which students looked forward; and they seldom failed to obtain from them ideas and what he himself called 'notions' that stimulated thought and discussion. His main original work—on the surgical anatomy of lymphatic areas in collaboration with the late Mr. J. F. Dobson—has stood the test of time. They employed Gerota's method of injection, and they published, as the fruit of much time-consuming labour, a series of papers, notably on the lymph-drainage of the tongue, stomach, and large intestine, that are now classical. Their principal illustrations of these organs are well known, as inevitably they found their way into the standard textbooks. It is to be regretted that Jamieson—immersed in affairs as he became—did not find time to carry out his intention to incorporate all their results in a volume which certainly would have worthily filled the gap that still exists for a work in English on the lymphatic system.

"Jamieson was an indefatigable and lively correspondent, and doubtless many of his friends possess and have been re-reading collections of his letters—informative, amusing, gossipy, often cryptic and not infrequently pungent in their comments on local and other affairs. In his later years, disabilities, which he had long suffered almost gladly, prevented him enjoying his regular round of golf; but that too became matter for amusing comment and, in spite of the increasing burden, his natural resilience appeared to be almost unabated. By his pupils, his colleagues, and his friends John Kay Jamieson will always be gratefully remembered as a notable and remarkable figure, whom to have known has indeed been a liberal education."

Professor Jamieson married Elisabeth, daughter of Dr. R. P. Goodworth. She died in 1936 and they leave a son and a daughter.

JAMES ERNEST HELME ROBERTS

O.B.E., M.D. LOND., F.R.C.S.

Mr. J. E. H. Roberts, consulting surgeon to St. Bartholomew's Hospital and emeritus surgeon to the Brompton Hospital, died at his home at Ottershaw on Aug. 25.

Roberts was educated at King Edwards' School, Birmingham, and St. Bartholomew's Hospital, where he qualified in 1906, graduating M.B. with honours in surgery two years later, and taking the F.R.C.S. in 1909. After holding house-appointments at St. Luke's Hospital and at Great Ormond Street, he became demonstrator in surgical pathology and chief assistant surgeon in the outpatients department at Barts and later surgical registrar and chief assistant in the orthopædic department. In 1919 he was elected assistant surgeon and in 1933 he was appointed to the full staff. He was also surgeon to the East London Hospital for Children.

During the first world war, during which he served with distinction, holding the rank of major and being thrice mentioned in despatches, he became interested in thoracic surgery. In 1919 he was appointed to the Brompton Hospital, and from this time his main energies were directed to this branch of surgery, to which he made considerable contributions, notably in the treatment of acute and chronic empyema. Roberts was the first to use active negative-pressure suction in these conditions, and his operation for the closure of old chronic empyema cavities has become the most efficient method at our command. His early reviews of one-stage lobectomy, published with the late H. P. Nelson, were a milestone in intrathoracic work.

A good teacher, he gathered a group of enthusiastic men around him, encouraging the younger men to further the work he had already done. One of these younger colleagues writes: "Those of us who knew Roberts in his later years respected, admired, and liked him for his pioneering spirit and for the rugged strength of his personality. When he joined the staff of Brompton Hospital surgery of the chest was practically confined to the drainage of empyema, and it was no easy task for the young surgeon to persuade his colleagues to try those operations which his experience in the 1914–18 war had suggested. No-one will ever know how much we owe to Roberts and how many of the operations which are now commonplace were the result of his pioneer work. His inquiring scientific mind enabled him to work out his techniques on a sound mechanical basis, and he was never happier than when arguing with the physiologists and applying their principles to his work. No surgeon ever worked more thoughtfully. He also had unique powers of observation, and those who went round the wards with him could not fail to be impressed by his clinical judgment; they always came away with some practical point to remember. Above all, Roberts was a fighter; his ideas were not always popular but he pursued them with courage and with a dry sense of humour which endeared him to his friends. He never avoided criticism, and was always prepared to produce a closely reasoned argument. All his friends will remember the backward tilt of his head and the triumphant twinkle in his eyes as he scored his point."

Roberts's interest in the scientific aspect of surgery was shown by the variety of scientific bodies with which he was associated. As one of its earliest presidents he gave the Society of Thoracic Surgeons considerable impetus, and more recently, from the chair of the Tuberculosis Association, he showed how admirably medicine and surgery could be blended in one person. To the Medical Society of London, over which he had also presided, he delivered in 1935 the Lettsomian lectures on

Digitized by Google

the surgery of pleural and pulmonary infection. A member of the International Association for Surgery, he was also a foreign associate of the Société Belge de Chirurgie, and an honorary fellow of the American Association of Thoracic Surgeons and of the Polish Society of Surgeons of Warsaw. A valued member of the Standing Advisory Committee on Tuberculosis from its inception to the time of his death, his advice on the surgical control of this problem was of the utmost importance.

With all his medical activities, he still found time for other interests, and he became a recognised authority on dragonflies and alpine plants. Till the beginning of the late war his holidays were spent in the Alps, and at his home he had a superb collection of these plants. C. P. T., to whom we are indebted for much of this memoir, adds: "Roberts was often brusque, almost to the point of rudeness, but those who knew him well fully appreciated the kindness which underlay his brusqueness. His apparent offhandedness could be attributed to his absent-mindedness; it was possible to talk to him for a considerable time without his being aware of it, and only persistent effort could break into these absent-minded periods. Once his attention was engaged he gave himself wholly to the matter in hand. All those who were privileged to know him will regret the passing of a loyal friend."

Another colleague, paying tribute to Roberts's contribution to chest surgery, continues: "His sanatoriums will sadly miss his regular visits which, though not always starting exactly at the appointed hour, were demonstrations of expert craftsmanship larded with intervals in which words of real wisdom and experience mingled with cigarette smoke. In debate or discussion his comments could be trenchant, but to the individual—and particularly to his juniors—he was invariably kind and helpful, and behind his reserve he was a most charming and gracious companion."

Mr. Roberts married Coral, daughter of the late Captain J. A. Elmslie, R.N.R., who survives him.

PERCY ROYCROFT LOWE

O.B.E., B.A., M.B. CAMB.

Dr. P. R. Lowe, formerly president of the British Ornithologists' Union and chairman of the European and British section of the International Committee for the Preservation of Birds, died on Aug. 18 at the age of 78. For many years he was in charge of the bird room of the British Museum (Natural History).

From Jesus College, Cambridge, he went to Guy's Hospital, where he qualified in 1897. After holding house-appointments at Leicester and Derby he went to South Africa in 1899 as one of the six civil surgeons chosen by the War Office to serve in the South African War. While medical officer in charge of a hospital train he began his collection of birds, and on his return from South Africa he was able to continue this work while acting as private physician to Sir Frederic Johnson, with whom he visited the West Indies. His collection of island forms of birds made during these voyages is now in the British Museum. During the 1914–18 war Lowe again commanded an ambulance train and for his services he was appointed O.B.E.

In 1918 his appointment as keeper at the British Museum enabled him to devote the rest of his life to ornithology. His work for the preservation of wild fowl was recognised by the award of the Swedish Verner von Heidenstam gold medal in 1939, and his researches in bird anatomy and classification by the Salvin gold medal in 1946. He also represented the Government and the Home Office at various ornithological congresses on the Continent.

A colleague writes: "A man of great charm and of fundamental kindliness, Dr. Lowe would take any amount of trouble to help anyone, and he was always ready to encourage those younger and less knowledgeable than himself. As a chairman his tact, sense of justice, and ability to see another's point of view, won the love and trust of his colleagues of other nations. Though ornithology was Dr. Lowe's chief interest he was a botanist of no mean order and his delight in finding a new plant never waned."

Notes and News

PRIVATE PRACTICE FROM HEALTH CENTRES

IN answer to an inquiry concerning a proposed experimental health centre at Stechford, Birmingham, the Minister of Health has informed the local executive council that doctors will not be allowed to treat private patients at centres set up under the National Health Service Act. The *Times* (Aug. 31) reports that the general-purposes committee of the council is seriously concerned at this ruling, and will recommend, at the first annual meeting of the Executive Councils Association, in London on Oct. 7, energetic measures to reverse the Minister's decision. A draft resolution to be submitted to the association expresses the view that if this decision is not reversed, it may be impracticable to operate health centres.

OPHTHALMIC PRESCRIPTIONS

THE method of writing an ophthalmic prescription generally accepted in this country and in the U.S.A. is:

Right Eye: Sphere..... Cylinder.....
Left Eye: Sphere..... Cylinder.....

A large firm of optical manufacturers points out that some doctors now practising in this country make out prescriptions in the reverse way, writing the cylinder before the sphere, and the left eye before the right. Often these prescriptions are passed on to manufacturers whose staffs are trained in the conventional method of composing them; so a large number of returns is incurred which could be avoided if all doctors adhered to the normal practice.

DEEPER AND DEEPER

THE "record" of 480 ft. for deep diving put up in 1945 by Arne Zetterstroem (*Lancet*, 1945, ii, 292) has been beaten by Petty Officer William Bollard, who reached a depth of 535 ft. in Loch Fyne on Aug. 28 (*Times*, Aug. 30). This dive was made in an Admiralty flexible deck diving-suit, and, in view of the fact that Zetterstroem died on the way to the surface, it is not surprising that Bollard, though he reached 535 ft. at 9.29 A.M., was not allowed out of the decompression chamber until 4.45 P.M. The previous "record" held by a diver who survived the ascent was that of Nohl, of Milwaukee, who reached 420 ft. in a diving-suit of his own invention (End, E. *J. Industr. Hyg.* 1938, **20**, 513). Petty Officer W. Soper also broke the American record on Aug. 28 by diving to 480 ft. It is but fair to say that Nohl's dive was limited by the depth of water in Lake Michigan. We are not told whether Bollard reached the bottom of the loch or not.

URINE TESTING WITHOUT HEAT

AN ingenious modification of Benedict's test for sugar in the urine is now available, in which no external heat is required. The test, known as 'Clinitest,' is carried out by placing five drops of urine plus five drops of water in a test-tube. One clinitest tablet is then added, a few seconds allowed to elapse for the reaction to occur, and the colour then compared with a colour chart. The tablet contains anhydrous copper sulphate, anhydrous sodium hydroxide, citric acid, and sodium bicarbonate. About half of the necessary heat is furnished by the heat of solution of the anhydrous sodium hydroxide and about half by the heat of the neutralisation reaction between sodium hydroxide and citric acid. Clinitest, which has been approved by the medical subcommittee of the Diabetic Association, is distributed by Don S. Momand Ltd., 57, Albany Street, London, N.W.1, from whom further details can be obtained. The complete set, including bakelite case, apparatus, and reagent tablets for 36 tests, costs 12*s*.

MEDICAL PROTECTION SOCIETY

FOR this society 1947 was a year of continued success and progress, during which 1501 new members were enrolled. It was also a particularly busy year because of the large number of questions about the new health service. In the annual report the society's solicitor comments on the growth in the number of needles broken during injection. In each instance where a metallurgist's report has been obtained a flaw in the metal has been found; but a word of warning is added on the adverse effect of iodine on steel. The society recently dealt with a case where a needle had broken because of pitting caused by iodine, in which it had been immersed for only a

Digitized by Google

very short time. "It is most important that practitioners should realise that iodine should not be used in connection with injections and that stainless steel needles should be kept away from all contact with iodine." The solicitor also remarks on the extraordinary increase, compared with pre-war years, in cases of fractured jaw due to tooth extraction. The council's decision to keep the annual subscription at £1 is a tribute to the health of the society's finances, for the annual cost per member has risen from 15*s.* 4*d.* in 1945 to £1 3*s.* 3*d.* last year. This increase is attributed to rising costs in general, and in particular to the award of much heavier damages by the courts.

J.A.M.A.

BRITISH readers of the *Journal of the American Medical Association* have been glad to see in the issue for Aug. 7, the latest to reach us, that the journal's printing troubles have ended.

University of Leeds

Prof. J. W. McLeod, F.R.S., is to succeed Prof. Matthew Stewart as dean of the medical faculty. Professor Stewart is retiring owing to pressure of other work. He has been academic subdean since 1923, and dean since 1941.

Prof. W. E. Le Gros Clark, F.R.S., is to give the inaugural lecture of the faculty of medicine at the University Union on Tuesday, Oct. 12, at 3 P.M. He has chosen as his subject Intellectual Adventure.

University of Aberdeen

Mr. W. O. Kermack, D.SC., F.R.S., has been appointed to the new MacLeod-Smith chair of biological chemistry. Dr. Kermack has been director of the chemical department of the research laboratory of the Royal College of Physicians of Edinburgh since 1921.

Royal College of Physicians of London

Dr. F. M. R. Walshe, F.R.S., will deliver the Harveian oration at the college, Pall Mall East, S.W.1, on St. Luke's day, Monday, Oct. 18. He is to speak on the Structure of Medicine and its Place among the Sciences.

Society of Apothecaries of London

Ten postgraduate lectures on modern therapeutics will be delivered in the hall of the society, Black Friars Lane, E.C.4, from Oct. 18 to Nov. 5. Further particulars will be found in our advertisement columns.

Institute of Laryngology and Otology

On Tuesday, Sept. 7, at 9.30 A.M., at the institute, 330, Gray's Inn Road, London, W.C.1, Mr. Myles L. Formby will give a lecture on Non-operative Treatment of Maxillary Sinusitis.

Tuberculosis Course

A refresher course for doctors on the treatment of non-pulmonary tuberculosis including lupus will be held at Lord Mayor Treloar Cripples' Hospital, Alton, Hants, from Oct. 5 to 7. Further particulars may be had from Dr. Harley Williams, N.A.P.T., Tavistock House North, London, W.C.1.

Congress of Obstetrics and Gynæcology

The twelfth British Congress of Obstetrics and Gynæcology will be held from July 6 to 8, 1949, in the Friends Meeting House, Euston Road, London, N.W.1, under the presidency of Sir Eardley Holland. Subjects already chosen for discussion include: Modern Cæsarean Section (opener, Mr. McIntosh Marshall); Essential Hypertension in Pregnancy (Prof. George Pickering and Prof. F. J. Browne); Diagnosis and Prognosis of Carcinoma of the Uterus (Dr. J. E. Ayre and Dr. F. G. Spear); and Maternal Mortality. The hon. secretaries would like to have the names of those who hope to attend not later than March 31.

Whitley Councils

Some of the Whitley council machinery described in our issue of May 29 (p. 845) is now in being. The general council, which will deal with questions affecting more than one group of workers, has not yet been established, but of the functional councils covering the different classes of people engaged in the health service the following have been or are being set up: optical, pharmaceutical, nurses and midwives, professional and technical grades (two councils, A and B). The membership of the medical and dental councils is still being discussed with the organisations concerned.

Edinburgh Post-Graduate Board for Medicine

On Friday, Sept. 10, at 3.30 P.M., in the anatomy lecture theatre of the university, Dr. W. Ritchie Russell will speak on Localisation of Cerebral Function.

North West Metropolitan Regional Tuberculosis Society

At a meeting of this society to be held on Oct. 6, at 4.30 P.M., at Colindale Hospital, N.W.9, Dr. H. M. C. Macaulay will open a discussion on the development of the tuberculosis service in the region.

Supplies of Diphtheria Antitoxin

Stocks of diphtheria antitoxin are now held by a few pharmacists and by infectious-disease hospitals. In centres where these hospitals are not readily accessible, the Ministry of Health has arranged for a small supply to be kept at a convenient general hospital.

Medical Films

The three morning film shows organised by the Scientific Film Association in connexion with the international scientific film congress will be held on Oct. 8 and 11 (cf. p. 360 of our issue of Aug. 28) at the Royal Society of Medicine, and on Oct. 9 at 1, Lambeth High Street, S.E. Applications for admission should be addressed to the organiser at 34, Soho Square, W.1.

Corrigendum.—The English publishers of Sulfonamides and Allied Compounds, by Dr. E. H. Northey, reviewed in our issue of Aug. 7 (p. 220), are Messrs. Chapman and Hall, and the price is 75*s.*

Appointments

HAYWARD, G. W., M.D. Lond., F.R.C.P.: physician for diseases of the heart, Southend-on-Sea General Hospital.
MATHESON, J. G., M.B. Aberd., D.A.: specialist anæsthetist, Royal Edinburgh Hospital for Sick Children.
MORGAN, N. H., O.B.E., F.R.C.S.: asst. orthopædic surgeon, Derby group of hospitals.
PRICE, D. E., M.B. Lond.: pathologist in the Home Office.

Births, Marriages, and Deaths

BIRTHS

BEVAN.—On Aug. 21, at Kyperounda, Cyprus, the wife of Dr. C. E. Bevan—a daughter.
BIRT.—On Aug. 25, at Godalming, the wife of Mr. St. John Birt, F.R.C.S.—a son.
BORLAND.—On Aug. 22, at Sunbury-on-Thames, the wife of Dr. A. K. Borland—a daughter.
CARTER.—On Aug. 24, in London, the wife of Dr. F. S. Carter—a son.
COCKBURN.—On Aug. 21, at Selsdon Vale, the wife of Dr. Hugh Cockburn—a daughter.
DENHAM.—On Aug. 22, the wife of Captain Robin Denham, R.A.M.C.—a son.
HALLETT.—On Aug. 27, at Lymington, the wife of Mr. Geoffrey Hallett, F.R.C.S.—a daughter.
KENNEDY.—On Aug. 20, at Penarth, South Wales, the wife of Dr. Michael Kennedy—a son.
LOUGHBOROUGH.—On Aug. 20, at Gosport, the wife of Dr. John Loughborough—a son.
MURPHIE.—On Aug. 28, in London, the wife of Mr. C. I. Murphie, F.R.C.S.—a daughter.
SOLOMON.—On Aug. 26, at Crendon, Bucks, the wife of Dr. R. M. Solomon—a son.
WADIA.—On Aug. 23, in London, the wife of Dr. Richard Wadia—a daughter.
WAUGH.—On Aug. 24, in Edinburgh, the wife of Dr. I. G. Waugh—a son.

MARRIAGES

DICKINSON—CARNEGIE.—On Aug. 24, at Baswich, Staffs, James M. Dickinson, M.B., to Ailsa Margaret Carnegie.
ROSS—WILSON.—On Aug. 26, at Arbroath, James McLean Ross, M.B.E., F.R.C.S.E., to Kathleen Margaret Wilson.

DEATHS

BROGDEN.—On Aug. 27, at Maybury, Woking, Surrey, George Alexander Brogden, M.A. Camb., M.D. Edin., aged 78.
BURTON.—On Aug. 23, at Frodsham, Cheshire, William Edward Burton, M.R.C.S., D.P.H., J.P., aged 82.
CARVER.—On Aug. 25, 1948, at Sutton Courtenay, John Roberton Carver, M.D. Camb., D.P.H.
LOWBURY.—On Aug. 24, in London, Benjamin William Lowbury, M.D. Berlin.
ROBERTS.—On Aug. 25, at Ottershaw, James Ernest Helme Roberts, O.B.E., M.B. Lond., F.R.C.S.
YOUNG.—On Aug. 28, at Tavistock, Augustus Henry Owen Young, L.R.C.P.I., lieut.-colonel, R.A.M.C. retd.

Digitized by Google

SEPT. 11, 1948 PAGES 401 TO 440

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6524 LONDON: SATURDAY, SEPTEMBER 11, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Modern Phonocardiography — G. E. DONOVAN, M.D. 401

Experimental Macrocytic Anæmia in the Rat — G. M. WATSON, M.B.; D. G. CAMERON, M.D.; Prof. L. J. WITTS, F.R.C.P. ... 404

Primary Tuberculosis with Meningism and Bacilli in the Spinal Fluid — Prof. K. CHOREMIS, M.D.; G. VRACHNOS, M.D. 408

Accidental Intra-arterial Injection of Drugs — S. M. COHEN, F.R.C.S. (*concluded*) 409

Acute Transverse Myelitis Complicating Pneumonia — A. I. SUCHETT-KAYE, M.D. ... 417

SPECIAL ARTICLES

Compensation for Injury — H. C. WARDLEWORTH NUTTALL, F.R.C.S. 425

Distribution of Streptomycin 428

The Birmingham Health Centre. 428

REVIEWS OF BOOKS

British Surgical Practice. Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., Prof. J. Paterson Ross, F.R.C.S. 418

Diagnostic Procedures in Virus and Rickettsial Diseases. T. Francis, jun. 418

Calcium and Phosphorus in Foods and Nutrition. Prof. H. C. Sherman 418

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 430

LEADING ARTICLES

PRIVATE PATIENTS IN HEALTH CENTRES 419

EXPERIMENTAL MEGALOBLASTIC ANÆMIAS 420

INTERNATIONAL INDUSTRIAL MEDICINE 421

ANNOTATIONS

Hospital-treated Sickness 422

Poisonous Berries 423

An Eagle in the Dovecotes 423

A New Disease ? 424

Glycosuria in Pregnancy 424

Birthday Greeting 424

Index to THE LANCET 424

DISABILITIES

12. Blindness 429

LETTERS TO THE EDITOR

Student Selection (Dr. Ff. Roberts: Mr. T. B. Layton, F.R.C.S.) 431

Binocular Microscopes (Prof. H. Hartridge, F.R.S.) 432

Plantar Warts in School-children (Dr. Melville Watkins) 432

Shoulder-girdle Syndrome (Dr. C. H. Davidson, Dr. N. S. Gordon) 433

Contraception in Germany (Dr. B. Sandler) 433

Family Periodic Paralysis 434

The Crossbow Outlet Pelvimeter (Mr. D. J. MacRae, F.R.C.S.E.). 434

Beds for Pulmonary Tuberculosis (Dr. M. M. Nagley) 435

Supernumerary Nipples (Dr. G. Dunderdale; Dr. Richard Harper) 435

Direct Reduction of Forward Dislocation of the Mandible (Dr. G. Maschanzker) 435

Sixty Years of Medical Defence .. 435

The Intending Emigrant (Mr. Archer Cust) 436

Association of Whole-time Salaried Specialists (Mr. R. C. Thomas, F.R.C.O.G.) 436

Hospital Libraries (Mr. W. R. LeFanu; Mrs. Buchanan) 436

The Deaf Child (Prof. W. N. Taylor, M.D.) 436

Shoulder Pain from Peptic Perforation (Mr. C. P. Sames, F.R.C.S.) 436

M.R.C.P. Examination 436

Urinary Incontinence in the Aged (Mr. D. F. E. Nash, F.R.C.S.) ... 437

Bovine Plasma (Prof. E. Carlinfanti, M.D., Dr. M. Pontecorvo) 437

Acute Benign Dry Pleurisy (Dr. A. Schrumpf) 437

Handling of Food (Dr. H. M. S. Turner) 437

PUBLIC HEALTH

Nightshade Poisoning 438

Notification of Infectious Diseases 438

OBITUARY

Thomas Gwynne Maitland 439

Andrew Radburne Fuller 439

NOTES AND NEWS

Case of Oscar Wilde 440

Option under Superannuation Regulations 440

Outpatient Facilities for Psychiatric Cases 440

Edinburgh Post-Graduate Board for Medicine 440

Institute of Laryngology and Otology 440

Institute of Psychiatry 440

International Congress on Industrial Medicine 440

Appointments 439

Births, Marriages, and Deaths ... 439

Founded 1892 Assets exceed £120,000

The MEDICAL PROTECTION SOCIETY Limited

President: SIR ERNEST ROCK CARLING, F.R.C.P., F.R.C.S., F.F.R.

Established for the protection of the professional interests of medical and dental practitioners. Members receive advice and assistance in all matters affecting the practice of their profession and are afforded COMPLETE INDEMNITY against costs and damages in cases undertaken on their behalf.

Entrance Fee 10/-

Annual Subscription £1 Membership Exceeds 23,000

No entrance fee to those joining within 12 months of registration

An additional subscription will secure indemnity in respect of practice overseas

Full particulars and application form from—

The Secretary, VICTORY HOUSE, LEICESTER SQUARE, W.C.2. GERrard 4553 & 4814

Digitized by Google

Published 1st September

THE BRITISH PHARMACOPŒIA 1948

45s. net. Postage: Inland 1s. 2d. Abroad 1s. 7d.

Published for

THE GENERAL MEDICAL COUNCIL

by

CONSTABLE & CO LTD LONDON W.C.2

10 ORANGE STREET

EXCERPTA MEDICA

FIFTEEN JOURNALS CONTAINING PERTINENT AND RELIABLE ABSTRACTS IN ENGLISH OF ALL ARTICLES IN THE FIELDS OF CLINICAL AND EXPERIMENTAL MEDICINE FROM EVERY AVAILABLE MEDICAL JOURNAL IN THE WORLD

Section I	Anatomy, Anthropology, Embryology and Histology	*Section VIII*	Neurology and Psychiatry
Section II	Physiology, Biochemistry and Pharmacology	*Section IX*	Surgery
Section III	Endocrinology	*Section X*	Obstetrics and Gynæcology
Section IV	Medical Microbiology and Hygiene	*Section XI*	Oto-, Rhino-, Laryngology
Section V	General Pathology and Pathological Anatomy	*Section XII*	Ophthalmology
Section VI	Internal Medicine	*Section XIII*	Dermatology and Venereology
Section VII	Pediatrics	*Section XIV*	Radiology
		Section XV	Tuberculosis

The Lancet. '. . . The difficulties of collecting, every month, several thousands of abstracts, all needing careful editing, and many requiring translation into English, are not small, but the first two sections to issue their maiden numbers—*Dermatology and Venereology* and *Radiology*—show that a high standard has been set, and it seems likely that the *Excerpta Medica* will prove an important agent for disseminating knowledge of medicine.'

The British Journal of Radiology. '. . . The conception and execution of the scheme should command nothing but the highest admiration. . . . The serious student of both diagnostic and therapeutic radiology will find this publication essential for keeping abreast of the literature because, indeed, it is impossible to conceive of any other way of doing so.'

Write for a prospectus, or specimen copy of the section you require to

DEPT. T., E. & S. LIVINGSTONE, LTD., 16-17, TEVIOT PLACE, EDINBURGH, 1

Sole distributors for Great Britain and the British Dominions

Digitized by Google

HISTORICAL BUILDING
DES MOINES, IOWA

MODERN PHONOCARDIOGRAPHY

G. E. DONOVAN
M.D., M.Sc. N.U.I., D.P.H.
MEDICAL OFFICER OF HEALTH, LLWCHWR AND GOWER; MEDICAL SUPERINTENDENT, GARNGOCH ISOLATION HOSPITAL, GLAM

MODERN American practice is to record the heart sounds (1) linearly, the vibrations due to the underlying cardiac action being portrayed as they exist on the surface of the chest; (2) stethoscopically, an oscillogram of the heart-sound vibrations being registered as they are transmitted to the ears by the orthodox acoustic stethoscope; and (3) logarithmically, to agree roughly with a competent auscultator's auditory perception of the heart sounds as heard through a stethoscope if the personal factors are omitted.

The "logarithmic" or, as it is sometimes called, the "human audiographic" phonocardiogram is somewhat a misnomer. It is a phonocardiographic term and is used by me in this limited sense. It means that added frequency distortion of such a character has been introduced into a stethoscopic phonocardiograph that the resultant phonocardiogram resembles approximately what the auscultator using the orthodox acoustic stethoscope recognises as normal. This term is customarily used in phonocardiography and has by now probably received sufficient sanction by usage to be accepted.

Each of these standard records can be correlated with the underlying cardiac action. There is no reason why other intermediate positions should not be used, but the linear, stethoscopic, and logarithmic phonocardiograms should be the standard ones.

THE PHONOELECTROCARDIOSCOPE

The details of my method have already been described (Donovan 1943a, b, c, d, 1944, 1945). The apparatus consists essentially of a double-channel electronic-valve amplifying unit fitted with frequency controls, intensity control, and tone-compensated volume control, a double-beam cathode-ray oscilloscope fitted with a long-persistence fluorescent screen, recording camera, headphones, and accessories such as a special crystal microphone, electrocardiographic leads, and photoelectric plethysmograph. Fig. 1 is a simplified schematic diagram of the apparatus.

The apparatus permits the direct, instantaneous, simultaneous, and constant viewing of a pair of cardiac phenomena such as the phonocardiogram and electrocardiogram, phonocardiogram and sphygmogram, &c., on the fluorescent screen of the cathode-ray oscilloscope at the patient's bedside without the necessity of photographic registration and consequent loss of time in developing film. The amplified heart sounds are heard through moving-coil headphones by one or many auscultators while the traces are being directly observed on the screen. The auditory and visual impressions can be simultaneously compared.

Fig. 2 shows the instrument in use, with a simultaneous logarithmic phonocardiogram of one cardiac area and that of another on the fluorescent screen of the double-beam cathode-ray oscilloscope as they appear for direct visual observation. The photograph had to be taken in dim light, because the exposure had to be a compromise between those required for the images on the fluorescent screen, the apparatus, and the patient.

Permanent graphic records can be made by focusing the camera on the fluorescent screen of the double-beam cathode-ray oscilloscope and photographing one traverse of the pair of cathode-ray spots as they appear for visual observation—opening the shutter at the beginning and closing it at the end of the traverse of the spots. Where permanent records are desired as a routine, the traces are recorded on moving film and the spots are stationary in the horizontal axis but oscillate in the vertical axis.

The apparatus can be calibrated by injecting a small known voltage into the input of the amplifier. A transparent ruled graticule in front of the fluorescent screen assists in quantitative measurement.

Special Microphone

The microphone consists essentially of a cartridge or diaphragm crystal unit mounted in a special airtight case. The diaphragm acts as an acoustic transformer which increases the coupling between air and crystal

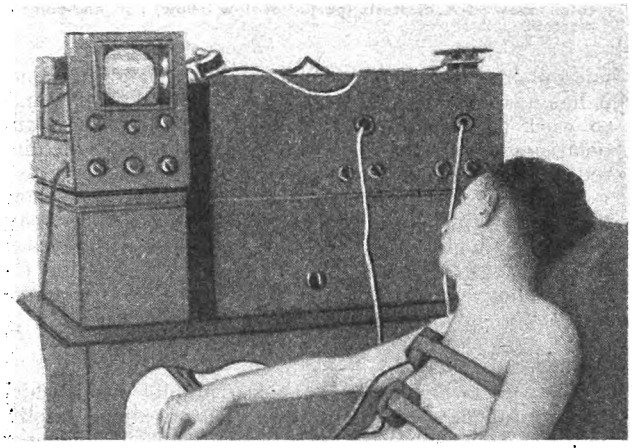
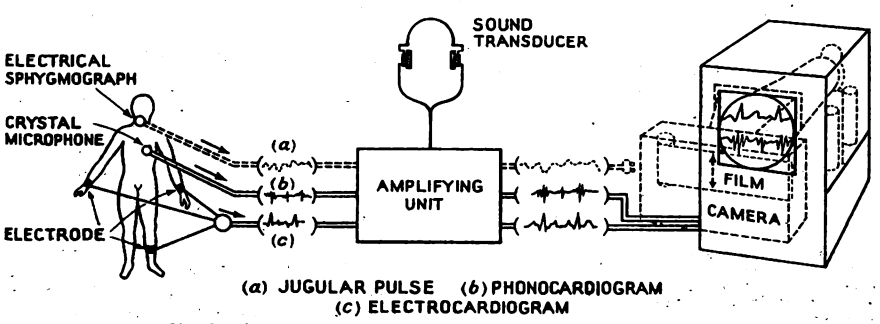


Fig. 2—Author's apparatus in use. Simultaneous logarithmic phonocardiogram of one area and logarithmic phonocardiogram of another area appear for direct visual observation on fluorescent screen.

and so increases the sensitivity. The air chamber in front of the diaphragm has an air-pressure equalising valve which connects the air of the space between the diaphragm and the patient's skin to the external air, and whose function is to protect the crystal from injury while the microphone is being applied to the chest wall. The valve is opened to allow the escape of the sudden high pressure while the microphone is being applied, but closed during the actual recording of the phonocardiogram. The chest-piece of the microphone is electrically insulated so as not to affect the registration of the electrocardiogram.

The natural period of the piezo-electric crystal incorporated in the microphone is about 10,000 cycles per sec.; but, owing to a diaphragm being coupled to the crystal, the natural period of the combination is lowered to a few thousand cycles per sec., which is well above the upper frequency limit of 1000 cycles per sec. for phonocardiography.

The microphone is sensitive and light, has a low parasitic background noise, and, unlike the carbon



(a) JUGULAR PULSE (b) PHONOCARDIOGRAM
(c) ELECTROCARDIOGRAM

Fig. 1—Simplified schematic diagram of phonoelectrocardioscope.

Digitized by Google

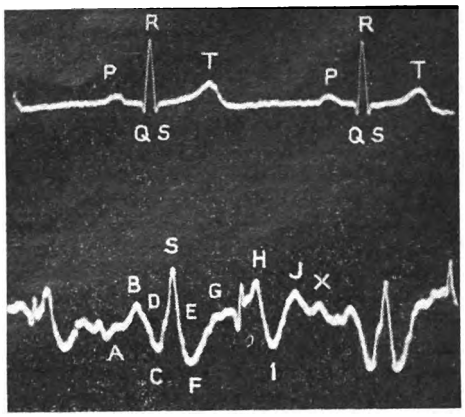


Fig. 3—Normal electrocardiogram lead 2 and jugular phlebogram (recorded by all-electric method) as they appear for direct visual observation on fluorescent screen. This type of jugular phlebogram, unlike electrocardiogram, demonstrates nearly every phase and event in cardiac cycle. Electrocardiogram lead 2 shows P, auricular wave; QRS, ventricular initial complex; and T, ventricular terminal wave. Jugular phlebogram shows different phases of systole and diastole: ABC, approximate duration of auricular systole (A-C interval); CD, isometric contraction; D, closure of A-V valves; S, interval of systole filled by large positive wave due to impact from adjacent artery; SE, sharp decline at onset of systolic ejection and descent of ventricular base; G, second heart sound; GH, phase of isometric relaxation; H, opening of A-V valves; HI, rapid ventricular inflow; I-X, diastasis (period of slow inflow); X, end-point of diastole.

microphone, is relatively unaffected by handling, since it has no loose granules. It has a suitable impedance to work without a transformer and does not require polarising potentials. The only type of shielding required is electrostatic.

The frequency response of the microphone is excellent for logarithmic and stethoscopic phonocardiography. The microphone's time constant is artificially increased by shunting with a 1 mF condenser in registering the linear phonocardiogram; this enables the microphone to register such slow pulses as the jugular pulse.

Amplifying Channels

There are two separate channels of amplifications which are resistance-capacity coupled. The maximal amplification of each channel is 500,000 times, and the frequency response is flat within ± 7½% between 0·15 and 5000 cycles per sec. Electric filters are incorporated which narrow down the frequency bands of observation to reduce the amount of extraneous and interfering variations outside the frequency range of interest. I prefer electric filters, unlike some American workers who use an acoustic high-pass filter incorporated in the case of the microphone. They get various degrees of filtering action by using four chest-pieces with such a microphone. The electric filters have the advantage that the microphone is left in situ, and it takes only a few moments to get 25 different combinations by rotating two switches.

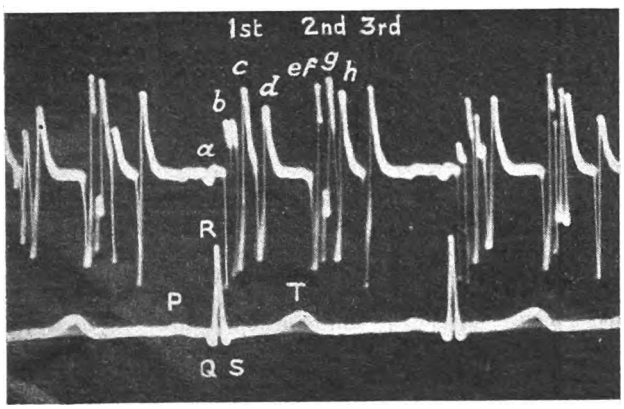


Fig. 4—Innocent triple rhythm in normal person. Record shows simultaneous stethoscopic apical phonocardiogram and lead I of electrocardiogram of a boy, aged 10 years, recorded on moving film. Stethoscopic phonocardiogram shows very well auricular complex of first heart sound. See text for explanation of record.

Double-beam Cathode-ray Oscilloscope

The cathode-ray tube is the most faithful recording medium available to the physiologist. Unlike other instruments used for this purpose (e.g., string galvanometer and mirror galvanometer) the moving part of the cathode-ray oscillograph—a stream of electrons—possesses practically no mass and is consequently practically without inertia. It can therefore respond faithfully to the most rapid variations of potential without overdamping or overshooting. It is immune from damage by deflectional overload. It is robust and easy to manipulate. The variations can be studied in relation to time by using a linear time base on the horizontal deflector plates of the cathode-ray tube.

The fact that the double-beam cathode-ray tube has two spots (which produce a long afterglow or phosphorescence lasting several seconds) capable of independent deflection in the vertical or Y-direction while being deflected simultaneously in the horizontal or X-direction from the left to the right borders of the fluorescent screen by a common time base permits direct visual, simultaneous, and continuous observation of two phenomena such as a phonocardiogram and electrocardiogram, or a phonocardiogram and sphygmogram. The speed of the time base can be varied to show from one to several heart cycles on the fluorescent screen. By varying the amplification of the amplifying channels and the speed of the time base, an expanded heart-sound oscillogram and electrocardiogram can be seen on the screen.

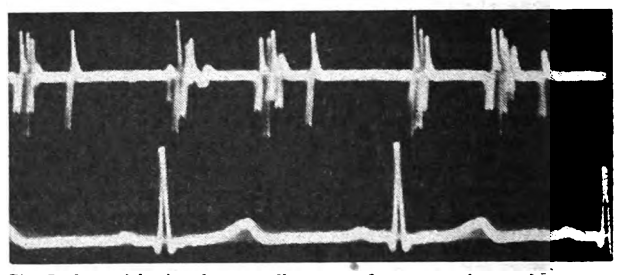


Fig. 5—Logarithmic phonocardiogram of same patient taken over same area as in fig. 4 and accompanied by lead I of electrocardiogram. This type of record agrees with auditory impression of auscultator but does not give so much information as does stethoscopic phonocardiogram. See text for explanation.

INTERPRETATIVE TRACES

It is desirable for the interpretation of the phonocardiogram to have it accompanied by a simultaneous electrocardiogram or phlebogram. The electrocardiogram is the more popular interpretative trace in this country, but the phlebogram has many advantages and its value is being increasingly recognised, especially in America.

Fishberg (1940) expresses the generally held view: "unfortunately to obtain a good tracing of the venous pulse is often a task of considerable difficulty, and the interpretation of the records is frequently obscure." Bramwell and King (1942) say that the method is chiefly of historical interest, since most information given by the phlebograph can now be obtained in a much clearer form with the electrocardiograph.

It must be pointed out that in many ways the electrocardiogram as a reference trace is not ideal, since the electrical manifestations of cardiac activity are not necessarily synchronous with the mechanical events. The

Digitized by Google

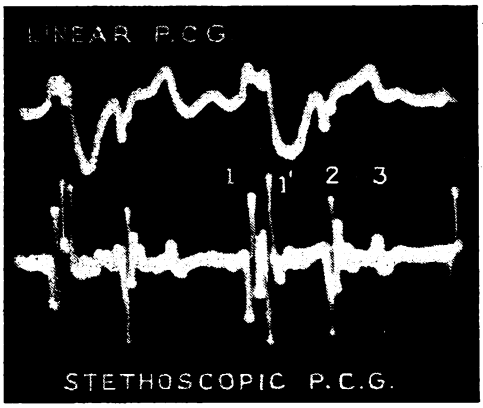


Fig. 6—Simultaneous linear phonocardiogram and stethoscopic phonocardiogram taken over apical area as they appear for direct visual observation on fluorescent screen, showing splitting of first heart sound. For explanation see text.

jugular pulse tracing with the latest technique gives something the electrocardiogram cannot give—i.e., mechanical evidence of the action of the heart chambers. It is a clinical method which produces a graphic record of nearly every phase and event during the cardiac cycle. The jugular pulse trace improves the possibility of analysing the phonocardiogram.

Fig. 3 shows the electrocardiogram lead 2 and the jugular pulse recorded with the crystal microphone, the capacitance of which was artificially increased by shunting an external fixed condenser across it. This is a photograph of the traces as they appear for direct visual observation on the long-afterglow fluorescent screen of my apparatus. It will be seen that the phlebogram gives much more information than does the electrocardiogram.

This electrical method has the advantages of comparative simplicity, great accuracy, elimination of rubber tubing, possibility of magnification as individually necessary, and possibility of synchronisation with other curves such as electrocardiograms, phonocardiograms, &c., recorded with more or less identical electrical methods.

I use the electrocardiogram as the routine interpretative trace for the phonocardiogram, but in difficult cases I prefer the jugular pulse tracing recorded by an all-electric method.

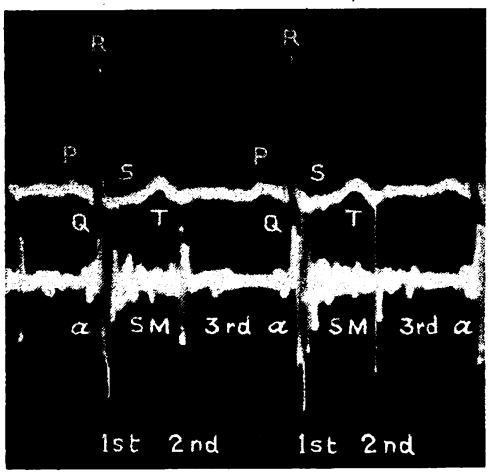


Fig. 7—Record of simultaneous electrocardiogram lead 2 and apical logarithmic phonocardiogram in mitral endocarditis in a woman, aged 20, as they appear for direct visual observation. Auricular complex (*a*) occurs between P and Q waves of electrocardiogram; central (*a*) complex is separated from first heart sound by an interval and is a form of presystolic gallop. First sound is accentuated and is followed by systolic murmur (SM). Second and third heart sounds are also seen. Diagnosis is mitral stenosis.

HEART-SOUND RECORDS

The following records were registered with the phono-electrocardioscope.

Case 1.—A stethoscopic apical phonocardiogram and lead 1 of electrocardiogram in a boy, aged 10 years, taken on moving film are shown in fig. 4. The first, second, and third heart sounds are clearly recorded.

The first heart sound has four components: *a*, due to auricular systole; *b*, produced at the beginning of the isometric contraction phase which finishes before the beginning of the ejection phase of ventricular systole; *c*, coincident with the onset of the ejection phase; and *d*, associated with the maximal ejection phase. The auscultator rarely hears the first and fourth components of the first heart sound: the sound he hears comprises the second and third components.

The second heart sound has four components: *e*, coincident with the beginning of the diastolic fall in pressure with relaxation of the ventricle; *f*, coincident with closure of the semilunar valve (end of ventricular systole); *g*, caused by vibrations in the arterial wall and in the aortic column of blood; and *h*, presumably caused by the opening of the mitral and tricuspid valves. The auscultator hears the second component of the second heart sound, but the first, third, and fourth components are attenuated or sometimes obliterated.

The third heart sound is registered well in the stethoscopic phonocardiogram, and its duration range is longer than by

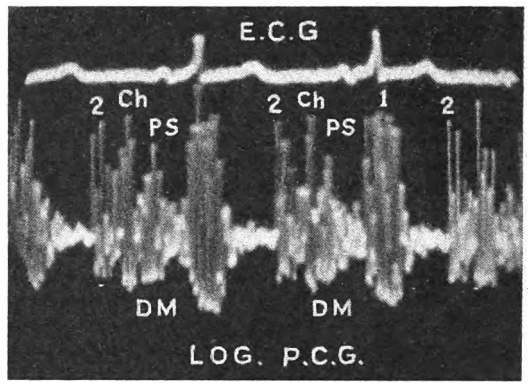


Fig. 8—Electrocardiogram lead 2 and apical logarithmic phonocardiogram in advanced mitral stenosis. Traces were photographed as they appeared for direct visual observation. 1 and 2, first and second heart sounds; Ch, opening snap of mitral valve; DM, diastolic murmur.

the logarithmic method. This sound is generally of low frequency and weak intensity. It is generally very difficult to hear by auscultation. The third heart sound is probably caused by vibrations of the ventricular walls due to their sudden distension by the onrush of blood from the auricles into the ventricles in the period of rapid ventricular filling.

A logarithmic phonocardiogram of the same patient taken over the same area and accompanied by lead 1 of the electrocardiogram is shown in fig. 5. This type of phonocardiogram tends to agree with the auscultatory impression of the auscultator. The logarithmic phonocardiogram tends to register the second and third components of the first heart sound—i.e., *b* and *c*—but obliterates the first and fourth components, since these are of low frequency. This means that an auscultator can very rarely hear the first and fourth components of the first heart sound. The second and third heart sounds are also affected in this type of recording.

Case 2.—A linear phonocardiogram and stethoscopic phonocardiogram taken over the apical area in a man, aged 20, are shown in fig. 6. The traces were photographed on still film as they appeared for direct visual observation. The linear phonocardiogram can register the first and fourth components of the first heart sound but not so well the second and third components. Third heart sound registers well in this type of record. The stethoscopic phonocardiogram shows splitting of the first heart sound, owing to an exaggerated separation of the two major components of the first sound, the isometric phase and the ejection phase components: this may often occur at the end of expiration. This splitting of the first sound may be, and is in this particular case, a purely physiological event.

Digitized by Google

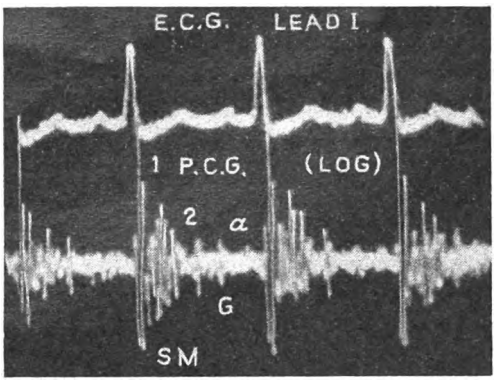


Fig. 9—Electrocardiogram lead I and apical logarithmic phonocardiogram in hypertensive heart disease: 1 and 2, first and second heart sounds; SM, systolic murmur; G, protodiastolic gallop; a, auricular complex. Traces were photographed as they appeared for direct visual observation.

Case 3.—An electrocardiogram lead 2 and a simultaneous apical logarithmic phonocardiogram in mitral endocarditis in a woman, aged 20, are shown in fig. 7. The traces were photographed on still film as they appeared for direct visual observation. The record shows an accentuated first heart sound, a form of presystolic gallop, systolic murmur, and second and third heart sounds.

Case 4.—A record of an advanced case of mitral stenosis in a woman, aged 30, is shown in fig. 8. It shows lead 2 of the electrocardiogram and an apical logarithmic phonocardiogram. The phonocardiogram shows the first and second heart sounds, the opening snap of the mitral valve, and a mid-diastolic murmur. The traces were photographed on still film as they appeared for direct visual observation.

Case 5.—Fig. 9 shows simultaneous electrocardiogram lead 1 and an apical logarithmic phonocardiogram in hypertensive heart disease, photographed as they appeared for direct visual observation. The blood-pressure was 230/140 mm. Hg. The phonocardiogram shows an accentuated first heart sound, a well-marked systolic murmur, and protodiastolic gallop rhythm.

Pulse Velocity.—By recording a simultaneous phonocardiogram or electrocardiogram with the finger-tip peripheral pulse one can time the interval between the beginning of the ejection phase of ventricular activity and the appearance of the pulse in the finger-tip. Fig. 10 is a record of an apical linear phonocardiogram and a peripheral pulse taken through the finger-tip in a man aged 40. The peripheral pulse has been registered by

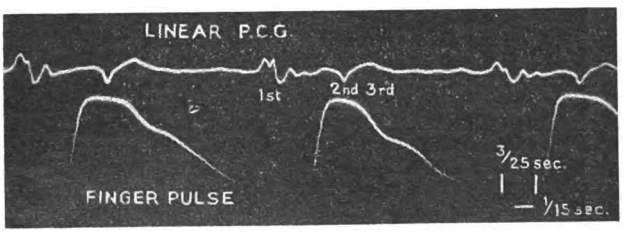


Fig. 10—Simultaneous linear apical phonocardiogram and peripheral finger-tip pulse recorded by author's photoelectric plethysmograph. Traces were photographed on moving film.

passing a beam of light through the tip of the index finger. The emergent beam strikes a photoelectric cell which changes any variations in the intensity of light into a corresponding variation in an electric circuit. The changes in light intensity vary with the changing blood-volume within the part. The electrical variations due to the varying translucency of the finger-tip are amplified by the second channel of the amplifying unit and are recorded on the fluorescent screen. The rate of propagation of the pulse is an index of the average elasticity of the arterial stem.

CONCLUSIONS

Much of the discussion by clinicians on phonocardiography is unsound because of their failure to recognise the important difference between heart-sound records registered by apparatus of widely different characteristics. Various types of phonocardiograms, such as the logarithmic, stethoscope, and linear, have not infrequently been erroneously compared as if they were the same in detail. It is possible that many of the inaudible vibrations which can be recorded may eventually prove to have almost as much clinical significance as have the cardiac sounds and murmurs.

The time has come when a committee should be set up for the standardisation of phonocardiographs. This standardisation should not be too rigid, since it could retard progress.

I wish to thank Mr. H. Marriott, B.ENG., B.SC.(ECON.), A.M.I.E.E., lecturer in electrical engineering at University College, London, for his help.

REFERENCES

Bramwell, C., King, J. T. (1942) The Principles and Practice of Cardiology. London.
Donovan, G. E. (1943a) *J. Inst. elect. Eng.* **90**, 38.
— (1943b) *Irish J. med. Sci.* p. 583.
— (1943c) *Med. Pr.* **209**, 298.
— (1943d) *Proc. R. Soc. Med.* **36**, 603.
— (1944) *Lancet*, i, 500.
— (1945) *Brit. med. Bull.* **3**, 137.
Fishberg, A. (1940) Heart Failure. Philadelphia; 2nd ed.

EXPERIMENTAL MACROCYTIC ANÆMIA IN THE RAT *

G. M. WATSON M.B. Adelaide, D.Phil. Oxfd
D. G. CAMERON M.D. McGill, B.Sc. Oxfd
L. J. WITTS M.D. Manc., F.R.C.P.
From the Nuffield Department of Clinical Medicine, The Radcliffe Infirmary, Oxford

STUDIES of the pathogenesis of pernicious anæmia have been hindered by our inability to reproduce the disease experimentally in an animal, and by the absence of a test for the therapeutic potency of liver extracts other than their clinical trial. Many tests have been suggested for the assay of liver extracts; King (1947) has reviewed these and points out that none has been proved of value. Castle's (1929) observations suggested that pernicious anæmia might be produced experimentally by resection of the stomach, but in practice experimental resections of the stomach, alone or accompanied by resection of part of the small intestine, have failed to produce the disease in the several species which have been used (Petri and Jensenius 1941, Jensenius 1945). In some recent dietary experiments (Cartwright et al. 1946, Welch et al. 1947) a macrocytic anæmia has been produced by adding a folic-acid antagonist to a purified diet. It is uncertain what relation this condition bears to the natural disease.

Another line of approach is suggested by the occasional association, in man, of anæmia closely resembling pernicious anæmia with gross intestinal disease. This has been known since Faber's (1897) report, and Barker and Hummel (1939) collected 51 cases of macrocytic anæmia in association with intestinal stricture or anastomosis. Other cases have been reviewed by Jensenius (1945). In anæmia of this type the blood picture is often indistinguishable from that of pernicious anæmia, and, where it has been examined, the marrow has usually been megaloblastic. The anæmia differs from pernicious anæmia in that achlorhydria and leuco-

* The expenses of this investigation were in part defrayed by a grant from the Medical Research Council.

Digitized by Google

penia are variable features, and the incidence of neurological disease is lower. Treatment with liver extracts is usually effective, as is surgical correction of the intestinal abnormality. In some of these cases steatorrhœa has been present, and the anæmia has been likened to that of sprue, but study of the case-records suggests that, though steatorrhœa is usual where there is a gastro-colic or high jejunocolic fistula, it is uncommon in other examples of this syndrome. A case under our own observation has shown that steatorrhœa is not an essential feature; in this patient megaloblastic anæmia followed an operation at which adjacent loops of ileum were anastomosed to by-pass a subacute obstruction from regional ileitis, but the output of fæcal fat, during a three-day balance experiment, was within the normal range.

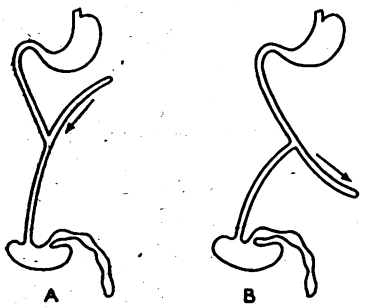


Fig. 1—Operations A and B, showing direction of peristalsis in loops.

Some early experiments suggested that it was possible to produce a similar condition in animals. Seyderhelm et al. (1924), by forming intestinal strictures in dogs, produced an anæmia with a blood picture resembling that of pernicious anæmia, and Tönnis and Brusis (1931) obtained similar results in dogs by forming blind intestinal loops.

This paper is an account of some experiments of this type, using rats as the test animal. We found that macrocytic anæmia may follow the formation of either a stricture or a blind intestinal loop; but as no reliable means could be found for producing a non-fatal stricture, loop formation was made the standard operation.

METHODS

The rats used in these experiments were albinos of Wistar strain and of either sex. The operations were done on rats aged 4–6 months; in rats of this age the blood-count has reached the normal adult level. The rats were maintained on a diet of casein, corn starch, and cod-liver and arachis oils, with mineral and vitamin supplements; this diet permitted normal growth and reproduction in intact animals, and control animals kept on it for a year did not develop anæmia. The composition of this diet, which was fed in excess, was as follows:

Corn starch	68%
Casein (unextracted)	25%
Cod-liver oil	2%
Arachis oil	2%
Salt mixture [1]	3%

Vitamin supplements:

Thiamine	100 μg. daily
Riboflavine	200 ,, ,,
Pyridoxine	100 ,, ,,
Calcium pantothenate	200 ,, ,,
Vitamin K	40 ,, ,,
Nicotinic acid	1 mg. ,,
Choline hydrochloride	10 ,, ,,

In addition vitaminised oil containing 2000 units of vitamin A and 200 units of vitamin D was given twice weekly, and 3 mg. of α-tocopherol was given once weekly.

It is probable (Jensenius 1945) that at least a third of the small intestine can be excised without serious effect on nutrition, and for the initial experiments the loop was made this length—about 12 in. Two types of operation were used: (1) in operation A the direction of peristalsis was such as to tend to empty the loop (fig. 1, A); and (2) in operation B peristalsis tended to fill the loop (fig. 1, B). In a later modification of operation B the length of the loop was reduced to 3 in.

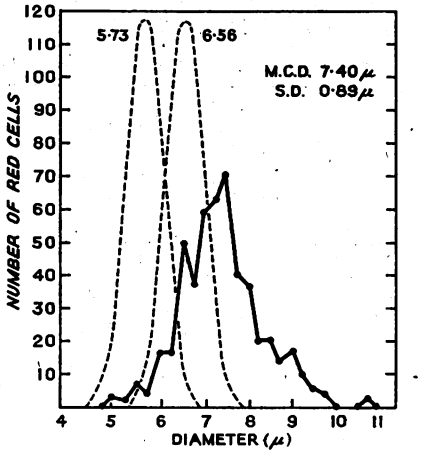


Fig. 2—Price-Jones curve from anæmic rat. Curve reveals macrocytosis and anisocytosis. Interrupted lines show limits of normal curves for rat blood, using Price-Jones convention of ±3 standard deviations.

RESULTS

Macrocytic anæmia followed each operation in a proportion of the animals submitted to it, and its characteristics were the same for each type of operation. It was found, however, that anæmia developed after operation A only when there was some stenosis at the site of anastomosis, leading to dilatation of part of the loop. For this reason operation B was adopted, and this gave a much higher proportion of anæmic animals, though the immediate mortality after this operation was higher owing to its technical difficulty. After this operation the loop always becomes dilated.

Of the rats prepared by operation A 118 survived its immediate effects, and 21 (18%) of these developed macrocytic anæmia, at times varying from six weeks to a year after operation. With operation B, using a long loop, the mortality by the end of three weeks approached 75%; and, though by that time nearly all the surviving rats had a macrocytic anæmia, the disturbances produced by so large a loop were excessive, and the rats could not be saved with liver extract. When this operation was modified by shortening the loop to 3 in., results were more satisfactory: of 24 rats prepared in this way 17 survived, and 13 of these have developed macrocytic anæmia at an average interval of 8 weeks after operation.

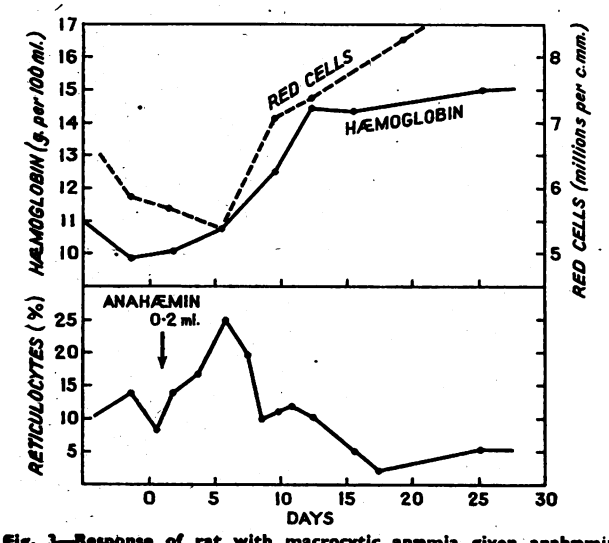


Fig. 3—Response of rat with macrocytic anæmia given anahæmin 0·2 ml. (operation A).

DESCRIPTION OF THE ANÆMIA

The normal hæmoglobin level in our rats is about 14 g. per 100 ml., and anæmia has not been diagnosed unless the hæmoglobin has fallen below 10 g. per 100 ml. In

1. As recommended by Hubbell et al. (1937).

Digitized by Google

practice it is found that the rats either remain well or become progressively and severely anæmic. The red cells, which are normally a little fewer than 9,000,000 per c.mm., often fall at the same rate as the hæmoglobin, with the result that the colour-index does not change, but in some rats there has been hyperchromia. A count as low as 3·3 g. of hæmoglobin per 100 ml. and 2,150,000 red cells per c.mm. has been found, but usually the rat dies before the anæmia becomes so severe.

The presence of macrocytosis has been shown by increases in the mean cell diameter and by an extension of the Price-Jones curve beyond the upper limits of normal, and confirmed in several cases by an increase in the mean cell volume. The normal mean cell diameter is 6·14μ, and in anæmic rats mean diameters as large as 7·40μ have been observed; the average increase is about 0·6μ. The normal mean cell volume is 49μ_3; readings of 70μ_3 or more were sometimes seen, but estimates of the mean cell volume are subject to considerable error, and increases in the mean cell diameter were not always accompanied by an increase in the mean cell volume. Anisocytosis was a striking feature of the anæmia, but poikilocytosis was never more than slight.

THE BLOOD PICTURE OF RATS WITH MACROCYTIC ANÆMIA

—	Hæmoglobin (g. per 100 ml.)	Erythrocytes (millions)	Reticulocytes (%)	Hæmatocrit (%)	M.C.H. (μμg.)	M.C.V. (c.μ.)	M.C.D. (μ.)
Normal mean	13·8	8·69	4	42	16	49	6·14
Anæmic rats							
1	10·0	5·70	3	28	18	49	6·46
2	8·5	3·80	27	27	22	71	6·99
3	3·3	2·15	14	—	15	—	7·40
4	8·8	5·60	10	31	16	55	6·73
5	8·3	4·56	15	—	18	—	7·09
6	8·7	5·80	10	31	15	54	6·44
7	5·8	3·32	27	22	17	66	6·44
8	8·8	7·40	11	42	12	57	6·42
9	8·6	4·13	18	23	21	55	6·50
10	7·0	4·80	21	—	15	—	6·60
11	8·3	5·00	22	29	17	58	—
12	4·9	3·35	40	18	15	54	6·38

The first 6 rats were prepared by operation A, and the last 6 by operation B.

The anæmic animals have an irregular reticulocytosis manifested in the stained films by increased polychromasia. Nucleated red cells were usually present in peripheral blood films. Leucocytes were present in normal numbers and did not show appreciable qualitative change. Some of these points are illustrated in figs. 5 and 6. In fig. 7 a blood film is shown from a rat with a hypochromic normocytic anæmia; this type of anæmia was occasionally seen after operation A only, and the appearance of the film is in striking contrast to that seen in macrocytic anæmia. These photomicrographs are all at the same magnification. Fig. 2 is a Price-Jones curve from a rat with macrocytic anæmia.

Once anæmia has appeared it usually progresses fairly rapidly if untreated, and the limit of survival appears to be about a month. A few anæmic animals prepared by the earlier technique had spontaneous remissions of their anæmia, but this has never happened after operation B. Animals with anæmia tend to lose weight and regain it with a therapeutic remission. They do not show any external evidence of deficiency disease. The

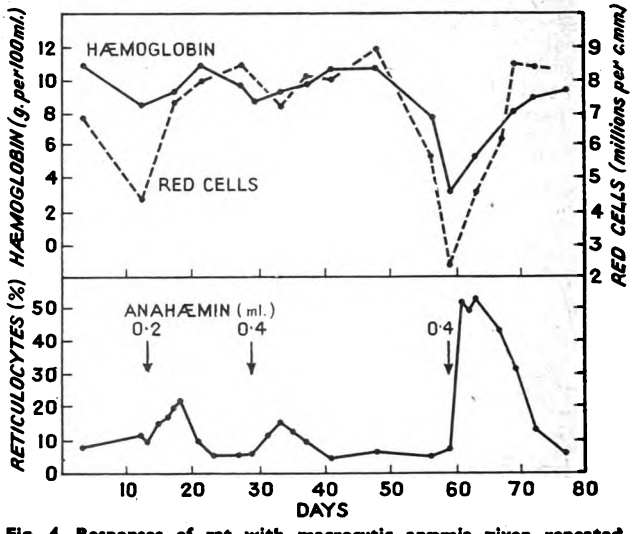


Fig. 4—Responses of rat with macrocytic anæmia given repeated injections of anahæmin (operation A).

accompanying table gives representative examples, at various levels, of the blood findings in animals with anæmia.

CHANGES IN THE BONE-MARROW

Bone-marrow smears were made from normal and anæmic rats by a method which did not involve sacrifice of the animal (Cameron and Watson 1948). Smears from rats with macrocytic anæmia showed normal or increased cellularity, and the most striking change in distribution was an increase in the proportion of earlier red-cell precursors. In smears from normal rats the predominant cells of the erythroblast series are small polychromatic normoblasts with dense or cartwheel nuclei; this distribution was unaltered in rats subjected to repeated hæmorrhage, but in rats with macrocytic anæmia there were increased numbers of pro-erythroblasts and basophil erythroblasts. The degree of this change varied considerably in different rats. No cells were seen which corresponded exactly to the megaloblasts seen in human pernicious anæmia, but there were some cells of the erythrocyte series which appeared abnormal in that the nucleus did not have the compact character seen in cells from normal marrow, and occasional cells had a closer resemblance to the megaloblast. Marrow from anæmic rats showed increased numbers of plasma cells, but there were no appreciable

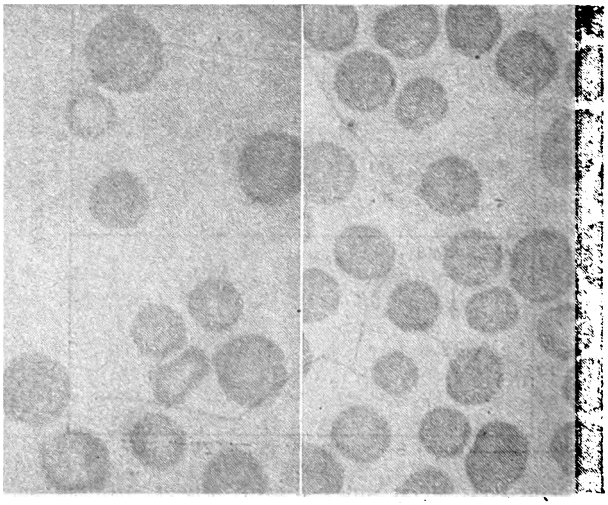


Fig. 5—Blood films from rat with macrocytic anæmia. (×1166.)

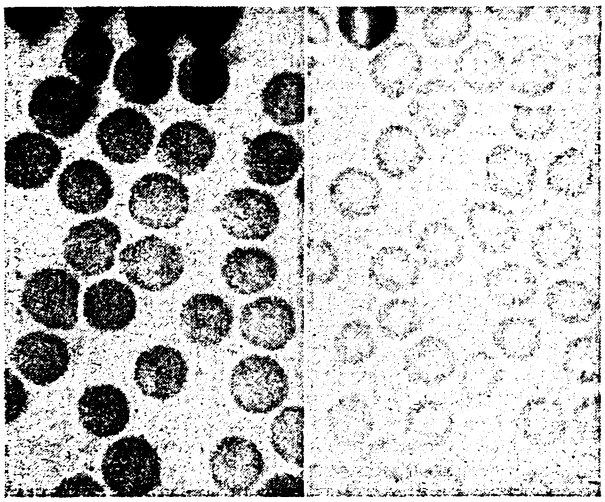
Digitized by Google

changes in the myeloid series. Figs. 8 and 9 are photographs of marrow from a normal rat and from an anæmic rat with a well-marked shift to the left of the red-cell series.

EFFECT OF LIVER THERAPY

If the rat is to be used as a test object for the anti-pernicious-anæmia principle or for similar purposes, it is important that the amount of the hæmoglobin should not be allowed to fall too low. The rat is a small animal with a brisk metabolism and does not tolerate anæmia well. If the hæmoglobin falls much below 7 g. per 100 ml. the rat becomes torpid and sleepy, its nutrition and resistance to infection are impaired, and the state of ill-health may become irreversible. For this reason tests are probably made best at a level of 7–9 g. of hæmoglobin per 100 ml.

A commercial preparation, 'Anahæmin,' was used to study the effect of liver extract on the macrocytic anæmia; the extracts which were used had been tested clinically in man and found to be active. Anahæmin was given by injection in doses of 0·1–0·4 ml. to 17 rats prepared by operation A; 10 of these showed a response to the liver extract. Of the 7 rats which did not respond



6 7

Fig. 6—Blood film from normal rat. (×1166.)

Fig. 7—Blood film from rat with hypochromic normocytic anæmia. This type of anæmia was seen occasionally after the earlier operation, but not after operation B. (×1166.)

4 had extensive septic infections and 2 had a fatal degree of intestinal obstruction. The observed responses to liver extract varied considerably in degree; the responses of 2 animals are shown in figs. 3 and 4. These results suggested that the anæmia responded to liver when it was not complicated by infection. More clear-cut results were obtained with rats prepared by operation B, with a 3-in. loop; there were no complicating infections in this group. From a group of 10 anæmic animals 5, chosen at random, were left untreated; these rats all died with a progressive anæmia, none surviving more than a month after anæmia was first noted. Of the remaining 5 rats 4 were given one or two injections of 0·4 ml. of anahæmin; these all showed a response to the liver and have remained alive and under observation for as long as eight weeks. The response to liver extract was again rather variable, 2 rats regaining completely normal blood-counts, while the other 2 had improved but still subnormal counts. The remaining rat of this group was injected with 15 mg. of synthetic folic acid; it too has shown a satisfactory response, the hæmoglobin and red-cell count rising nearly to normal in fourteen days. More observations are necessary to determine the

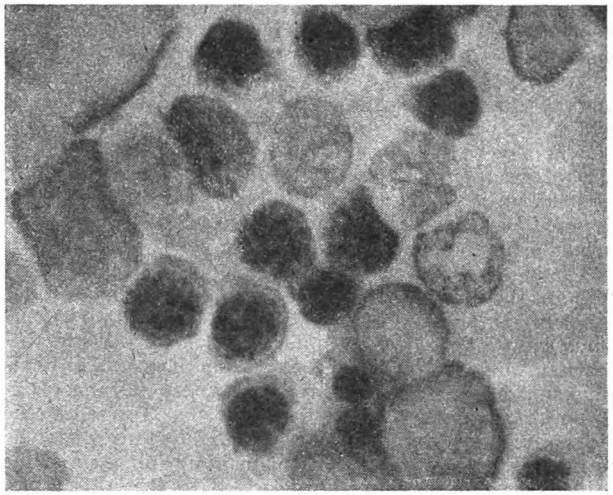


Fig. 8—Marrow smear from normal rat. (×1166.)

optimum dose of liver extract. These preliminary observations suggest that, when an adequate dose of liver extract is given at a level of 7–8 g. of hæmoglobin per 100 ml., reticulocyte increases of about 20% may be expected. The red-cell count rises at a rate of about 2,000,000 per c.mm. per week, though the hæmoglobin tends to lag behind. The most striking reticulocyte responses were seen in the rats prepared by operation A. In the more acute anæmia which follows operation B there is a greater reticulocytosis in the untreated animal; in these rats the reticulocyte percentage rose by a similar amount, but the higher initial count made the response less striking.

DISCUSSION

Several types of operation have been tried in these experiments. All of them may be followed by macrocytic anæmia, but only in the case of a 3-in. loop made to fill by peristalsis was there a high incidence of anæmia accompanied by a reasonably low mortality. We have made some experiments to determine the most useful site for the loop, and have found that the exact position is unimportant provided that it is in the upper or middle part of the small intestine. In a small group of animals, in which the loop was placed immediately above the cæcum, no anæmia has developed.

An unexpected feature of the animal anæmia was the large dose of liver extract necessary to produce a

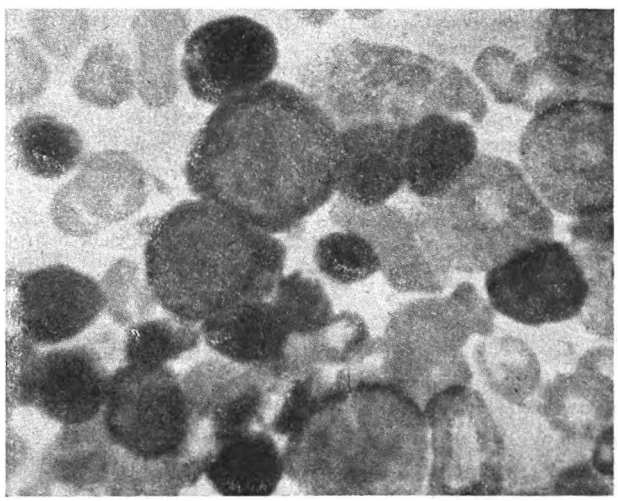


Fig. 9—Marrow smear from rat with macrocytic anæmia. (×1166.)

Digitized by Google

remission. Our impression is that the size of the dose depends on the size of the loop and on the rapidity of onset of the anæmia, but in any case at least 0·1 ml. of anahæmin was necessary to produce a remission, and in some cases as much as 0·8 ml. The manner in which liver extracts produce their effects is unknown, and it may be that calculations based on the weight of the animal are unreliable. A further point is that possibly, in small animals like the rat, the life span of the red cell is much less than in man, and the need for hæmopoietic principle may be correspondingly greater.

The anæmia seen in these rats resembled in most of its features the anæmia observed in human cases of intestinal stricture or anastomosis, and probably the two conditions are produced by a similar mechanism. What this mechanism is, and what is the relation of anæmia of this kind to Addisonian pernicious anæmia, remains uncertain. A working hypothesis is that materials are formed in the stagnant loop which in some way interfere with the formation, absorption, or utilisation of hæmatinic principles, and experiments designed to test this hypothesis are already planned. Diarrhœa was not present, and no symptoms of neuropathy were seen. Fat-balance experiments and the results of examination of the nervous system will be reported later.

A good deal of experimental work in animals has been confused by the presence of latent bartonella infections, which become manifest after splenectomy. However, we have no reason to believe that our rats had bartonellosis, or that bartonella infections can be activated in so specific a way by the formation of a dilated blind loop of intestine. Perla and Gottesman (1932) reported that a dietary supplement of copper and iron in amounts of 0·1 and 1·0 mg. respectively daily protected rats from bartonella infection, and the diet for the present experiments included these supplements. Finally, bartonella infection does not respond to liver in this way.

We have also not yet had opportunity to discover how specific is the response to liver and folic acid in these rats. The only other material with which we have experimented is pantothenic acid, and this was without effect. We have published the results obtained to date because they have already been reported at scientific meetings in this country and have attracted a good deal of interest. They seem to offer the promise of a reliable method of assay of liver extracts. They certainly provide a preparation which should be of value in revealing the mechanism of pernicious anæmia and allied megalocytic anæmias, which at present seems so complicated and obscure.

SUMMARY

The formation of a blind intestinal loop in the rat causes a macrocytic anæmia which responds to treatment with liver extract.

The pathogenesis of this anæmia is not yet known, but it depends on dilatation of the blind loop, with accumulation within it of intestinal contents.

The technique described is likely to be useful in the bio-assay of liver extracts and in analysing the mechanism of pernicious anæmia and allied megalocytic anæmias.

We are greatly indebted to Miss A. Hogg, Miss B. Mallet, Miss C. Stayte, and Mrs. M. Bruce-Lockhart for their help in this investigation, which has necessitated much tedious work in the care of the animals and in making blood examinations.

REFERENCES

Barker, W. W., Hummel, L. E. (1939) *Bull. Johns Hopk. Hosp.* **64**, 215.
Cameron, D. G., Watson, G. M. (1948) *Blood*, **3**, 292.
Cartwright, G. E., Wintrobe, M. M., Humphreys, S. (1946) *J. Lab. clin. Med.* **31**, 423.
Castle, W. B. (1929) *Amer. J. med. Sci.* **178**, 748.
Faber, K. (1897) *Berl. klin. Wschr.* **34**, 643.
Hubbell, R. B., Mendel, L. B., Wakeman, A. J. (1937) *J. Nutrit.* **14**, 273.
King, H. K. (1947) *Edinb. med. J.* **54**, 50.

References continued at foot of next column

PRIMARY TUBERCULOSIS WITH MENINGISM AND BACILLI IN THE SPINAL FLUID

SIGNIFICANCE IN STREPTOMYCIN TREATMENT OF TUBERCULOUS MENINGITIS

K. CHOREMIS
M.D. Athens
PROFESSOR OF PÆDIATRICS AND DIRECTOR OF PÆDIATRICS CLINIC, UNIVERSITY OF ATHENS

G. VRACHNOS
M.D. Athens
ASSISTANT PROFESSOR OF PÆDIATRICS UNIVERSITY OF ATHENS

IN an address on tuberculosis in childhood, given to the Greek Pædiatric Society in February, 1946, we discussed two new forms of the primary complex (the pyuric syndrome and the form with intermittent fever) and also described some associated manifestations in the central nervous system. We reported that 2 of our cases developed convulsions with each rise of temperature. In 3 other cases we noted exaggerated reflexes, which at times reached the stage of ankle clonus. Since such phenomena mean irritation of the pyramidal tract, their presence in the course of an acute primary infection led us to fear that tuberculous meningitis was imminent. However, it fortunately did not follow. Examination of the cerebrospinal fluid (C.S.F.) showed occasional rises in tension but no other abnormality either in composition or in cell-count. The neurological signs gradually subsided with the regression of the fever, malaise, &c., and disappeared.

These cases have been succeeded in our experience by others, and a similar case in an infant has been described by Dr. Zervos, assistant professor of pædiatrics in Athens, in a thesis dated 1947. There seems to be no doubt that they represent meningism during the primary infection, and we believe the explanation is a serous reaction of the meninges during the hyperergic period of the disease.

The appearance of meningitic signs which do not go on to tuberculous meningitis is of both theoretical and practical importance. It supports the view that during the course of tuberculous infection in childhood a local inflammatory reaction occurs on a specially allergic ground. This meningeal reaction does not develop clinically beyond the stage of slight meningism, either because it is limited and remains in the stage of simple inflammatory reaction, or because the development of tubercles is also limited and does not spread. Laboratory findings show only "a slight degree of hydrocephalus due to oversecretion by the choroid plexus."

Lincoln [1] refers to this type of meningeal reaction, with no changes in the C.S.F. except slight increase in pressure and in cell-count, *but with tubercle bacilli present.* This means that the presence of the tubercle bacillus in the C.S.F. does not always imply the development of meningitis in its full form. We have had 2 similar cases under our care.

CASE-RECORDS

Case 1.—A boy, aged 11 months, entered our clinic on Jan. 16, 1948. His mother said that a month earlier the

1. Lincoln, E. *Amer. Rev. Tuberc.* 1947, **56**, 75.

DR. WATSON AND OTHERS: REFERENCES—*continued*

Jensenius, H. (1945) Results of Experimental Resections of the Small Intestine on Dogs. Copenhagen.
Perla, D., Gottesman, J. M. (1932) *J. exp. Med.* **56**, 783.
Petri, S., Jensenius, H. (1941) *Acta med. scand.* **10**, 274.
Seyderhelm, R., Lehmann, W., Wichels, P. (1924) *Klin. Wschr.* **3**, 1439.
Tönnis, W., Brusis, A. (1931) *Dtsch. Zeit. Chir.* **233**, 133.
Welch, A. D., Heinle, R. W., Sharpe, G., George, W. L., Epstein, M. (1947) *Proc. Soc. exp. Biol., N.Y.* **65**, 364.

Digitized by Google

child was ill with bronchopneumonia and enterocolitis. After the acute illness he had not fully recovered; and on the day before admission he developed cough and anorexia, and became febrile and restless.

Examination.—Under weight (17 lb. 3 oz.), pale, and restless. Slight nuchal rigidity; tendon reflexes exaggerated. Lungs normal.

Investigations.—Blood: red cells 3,800,000 per c.mm.; white cells 13,500 per c.mm. (polymorphs 46%, lymphocytes 52%). Blood-sedimentation rate (Linzenmeier) 10 mm. Mantoux reaction (1/10,000) +++. C.S.F. (cisternal puncture): under normal pressure, clear; protein 20 mg. per 100 ml.; cells 8 per c.mm.; glucose 40–50 mg. per 100 ml.; chlorides 540 mg. per 100 ml.; tubercle bacilli present on culture. Urine normal. Radiographic examination of chest: bilateral hilar adenitis.

Progress.—Pyrexia continued for 5 days, and then slowly subsided. The patient was discharged after 15 days, clinically improved, with the diagnosis of tuberculous adenitis and meningism. He was followed up at home and seemed well. Lumbar puncture was performed on Feb. 26 (40 days after admission); the C.S.F. was normal in all respects, and on culture no tubercle bacilli were found. When seen four months later, the child appeared perfectly well, and physical examination revealed nothing abnormal.

Case 2.—A boy, aged 2 years; only child. Parents healthy, but an uncle with pulmonary tuberculosis had come to live in the home a few days after patient's birth. Birth-weight 8 lb. 11 oz.; B.C.G. vaccination not undertaken; breast-fed for six months. After the fourth month became mildly pyrexial, and during the previous week temperature rose to 100–101°F, on which account he was admitted on March 15, 1948.

Examination.—Nutrition poor, mucosæ pale. Tongue coated; tonsils slightly injected; liver just palpable; spleen enlarged 2 fingerbreadths below costal margin. Heart, lungs, and central nervous system normal. Lymph-glands not palpable.

Investigations.—Blood: red cells 3,500,000 per c.mm.; white cells 12,600 per c.mm. (polymorphs 36%, lymphocytes 60%, large monocytes 4%, normoblasts 1–2%). Sternal puncture: no leishmania or malarial parasites. Mantoux reaction (1/1000) ++. C.S.F.: pressure slightly increased, clear; protein 20 mg. per 100 ml.; cells 1–2 per c.mm.; tubercle bacilli not found on direct smear, but present on culture. Urine normal. Radiographic examination of chest: left hilar adenitis.

Progress.—Pyrexia persisted. General condition satisfactory; no vomiting or constipation. Patient complained only once of headache. From four days after admission given streptomycin intramuscularly 0·15 g. four times daily for a week; total dosage 4·5 g. After the first dose of streptomycin the temperature became and remained normal. Discharged on March 26. Two and a half months later clinical findings normal. Parents objected to further lumbar puncture.

DISCUSSION

There seem to be two possible explanations for such cases as these: (1) tubercle bacilli circulate in the C.S.F. without there necessarily being a focal lesion with its clinical sequelæ; or (2) the bacilli derive from a focus in the meninges which is too small to cause clinical manifestations, does not enlarge, and eventually recedes and disappears. Both explanations are feasible, but the second seems to be the more likely.

This problem is connected with that of the clinical reactions and laboratory findings in tuberculous meningitis treated with streptomycin, about which these further questions have to be answered:

1. Why do some cases respond immediately to streptomycin, whereas others respond slowly, and still others not at all?
2. Why is clinical improvement sometimes not accompanied by parallel change in the C.S.F., the abnormality of which persists?
3. What is the criterion of cure (if we can speak of "cure")? Does it rest on the clinical condition, on laboratory findings, or on negative results of culture for the tubercle bacillus?

In practice the most urgent question is the third; and we consider that the return of the cells and chemical state of the C.S.F. to normal is more significant than a negative culture. In 2 cases of another series, where the patients were discharged from the clinic as "recovered," culture of the C.S.F. a few days before discharge was positive for tubercle bacilli; and yet six months later both children appeared perfectly well. Clearly streptomycin is forcing us to review our earlier conceptions of the pathogenesis and development of tuberculous meningitis.

SUMMARY

Two cases are described in which tubercle bacilli were isolated from the C.S.F., without accompanying manifestations of tuberculous meningitis.

Both patients, one of whom received streptomycin, survived, and they were well 4 and $2^1/_2$ months later.

In the C.S.F. tubercle bacilli may sometimes either (1) exist without any focal lesion in the brain or meninges; or (2) derive from a minimal meningeal lesion which resolves. The second explanation seems the more likely.

It is suggested that in assessing "cure" of tuberculous meningitis greater weight should be attached to chemical and cytological findings in the C.S.F. than to the results of culture for the tubercle bacillus.

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SOL. M. COHEN
M.A. Cape Town, F.R.C.S.
CONSULTANT SURGEON, GRAVESEND AND NORTH KENT HOSPITAL, GRAVESEND; FORMERLY SURGEON, SOUTHERN HOSPITAL, DARTFORD, KENT

(*Concluded from p. 371*)

DANGERS OF THERAPEUTIC OR DIAGNOSTIC INTRA-ARTERIAL INJECTIONS

Tragedies following the intra-arterial injection of therapeutic substances or contrast media for radiography have also been collected in the hope that they may throw some light on the pathology and indicate the treatment. Gangrene of the fingers has followed accidental injection of iodoxyl for pyelography (B. Johnson, personal communication); sodium tetrachlor-iodophenolphthalein for cholecystography (S. I. Levy, personal communication); iodides for arteriography (White 1935); diodone injected into the femoral artery for leg arteriography has ended disastrously (Maybury 1946); and ethanolamine injected into the femoral artery instead of into varicose veins necessitated a high amputation of the thigh (Medical Defence Union 1947).

Levin and McElroy (1944) have described a case of cerebrospinal fever with thrombosis of the right axillary artery, followed by gangrene of arm and forearm. The patient, who was at first unconscious, received therapeutic intermittent intravenous injections of sulphapyridine into affected arm. Levin and McElroy agree that the gangrene is difficult to explain but admit that intra-arterial injection was a possibility. The pH of sulphapyridine is about the same as that of thiopentone, and its destructive effect, when it is injected in the region of nerves or into the spinal canal, is known to have caused several tragedies (Roberts 1942).

Gangrene of the hand has followed the injection of quinine. I am indebted to Mr. Frank Nicholson for the following case-report:

A patient with malign tertian malaria was admitted more or less in coma into a hospital in Tripoli. Intravenous quinine was required, and in the ensuing struggle the left brachial artery was probably punctured. I was asked to see the patient next morning, when the left hand was cold, white, and anæsthetic up to the wrist, and the radial pulse was absent. Exploration under general anæsthesia showed a hæmatoma beneath the deep fascia. The brachial artery was narrowed to the size of the radial artery, and there was a definite needle puncture in its anterior wall. Two inches of brachial artery was resected; local and stellate ganglion procaine block. The ultimate result is uncertain, for Mr. Nicholson embarked next day for Sicily; but I understand from a colleague attached to the same

Digitized by Google

division that amputation through the forearm became necessary.

Sir Philip Manson-Bahr informs me that he has heard of no similar tragedy with quinine, nor have the Army and other tropical disease authorities. Schmuttermayer (1936) records a "burning sensation in the hand" following intramuscular quinine on the outer side of the mid-arm; radial nerve-palsy followed, but the symptoms suggest some intra-arterial injection as well. "Malarial gangrene" of the foot, in a previously healthy man of 42, has been recorded (Leo 1937); but this complication has ensued usually only in neglected cases (Manson-Bahr, personal communication). Samuels (1945), describing malarial gangrene, states "it is usually caused by thrombosis of the arteries—the brachial artery is often involved"; such accidental intra-arterial injection may have been overlooked.

Extramural spilling of neoarsphenamine is well known to be followed by local sloughing. The intra-arterial accident seems to have been rare, for Dr. V. E. Lloyd, who is in charge of a V.D. clinic at Guy's Hospital, writes in a personal communication (1945): "No instance has happened in my hands or in the hands of anyone working with me. I have never heard the 'accident' referred to at meetings of the Medical Society for the Study of V.D. throughout the last twenty years."

Walsh and Wyatt (1945) have recorded a case in which arsphenamine hydrochloride ('Mapharsen') caused flushing and nothing else. I have traced a case where gangrene followed the accidental injection of arsphenamine ('Salvarsan'); the amputated forearm is in St. George's Hospital museum:

A man, aged 50. "No difficulty was noticed with the injection, and no unusual symptoms occurred at the time. After a few days pains started in the hand, which became swollen, with brawny œdema extending 3 in. above the elbow. The diagnosis of brachial artery thrombosis was made and the arm later amputated. A recent thrombus filled the brachial artery from a point 3 in. above its bifurcation downwards. Section showed slight endarteritis. There was no evidence of wounding of the artery or escape of salvarsan into the tissues."

Gammel (1927) has recorded extensive gangrene of the buttock following the "intramuscular" administration of bismuth. He reviews the literature, which includes several such cases, and shows that the effects were due to the injection into the inferior gluteal artery.

A particular feature of one of the cases he describes was the development of foot-drop. This neurological information is important, for the inferior gluteal artery is the main artery of supply to the sciatic nerve, and experimentally Okada (1905) showed that ligature of the inferior gluteal artery of a rabbit was followed by paralysis of the sciatic nerve.

This case is thus the first clinical confirmation of the profound effect of a single regional vessel on its nerve of supply, and provides the evidence that Adams (1942), in an exhaustive paper on the blood-supply of nerves, was seeking. It also appears to confirm the view already put forward that some of the effects in the thiopentone cases are due to thrombosis spreading to the vessels of supply of the major nerves of the forearm.

The hazards of the use of sclerosants during anæsthesia, as in the treatment of varicose veins, has been receiving increasing attention in recent years. Anæsthetists need to be acquainted with the fact that under general anæsthesia, with the limb immobile, injection of sclerosants into the superficial veins may be followed by thrombosis of the deep veins, owing to the numerous deep connecting branches. The pulmonary embolus, occasionally following the Trendelenburg ligature operation, is believed to be derived from this, rather than small clot remnant at the saphenous ligature stump.

The danger of such thrombosis is greatest if injection is done with the patient under general anæsthesia; if the operation is done under local anæsthesia, immediate muscle movement will sweep away the sclerosant. Those associated with medicolegal societies also know that arteries round the ankle have been accidentally injected (D. H. Patey, personal communication).

Gangrene of the hand and forearm has followed the injection of 'Myanesin' (Ogilvie et al. 1948), a particular feature of the case being the presence of good radial and ulnar pulses palpable through the gangrenous tissues. Ogilvie et al. demonstrated, in vitro, the "curdling" colloid precipitate effect of the admixture of blood and myanesin; with intra-arterial injections showers of coagula are swept into the distal stream to block, in mechanical fashion, the distal minute arterioles.

Numerous tragedies have followed the use of contrast media for arteriography, and Wagner (1944), reporting a case following the use of iodoxyl has given an admirable and comprehensive account of the literature.

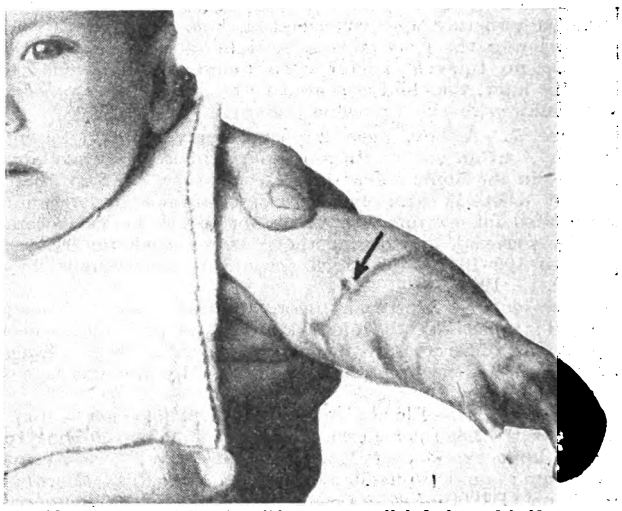


Fig. 21—Gangrene following "intravenous" infusion of half-strength Hartmann's solution plus 5% glucose in a baby, aged 6 months, admitted with diarrhœa and vomiting. Cannula had been introduced with difficulty into "vein" (indicated by arrow) on radial aspect of forearm. Oscillation of fluid in drip chamber had been noted, but had ceased on release of strapping holding arm to splint. (Case seen in consultation.)

Lambret (1935), Dos Santos (1935), and Leclerc (1935) have all given accounts of such tragedies. Leveuf (1935), in the study of one such case after iodoxyl in a child (and many of the tragedies have been in children), found a recent thrombus in the brachial artery, and observed that (as in some of the thiopentone cases) "no lesion could be found in the vicinity of the site of puncture." He did some experiments on the effects of irritants on vessels of bats' wings, the tongue of newts, and mesenteric vessels of rabbits, and concluded that "the normal rhythm between the arterioles and venous side of the capillary loop was disturbed. That led to gangrene." It is well to observe that, in this country, diodone ('Per-Abrodil' and 'Pyelosil') has in recent years been used for arteriography in hundreds of cases; the injection has been frequently repeated, and the result of my repeated inquiries from fellow workers appears to indicate that these media are absolutely safe.

Gangrene of the hand and forearm has followed the intra-arterial injection of Hartmann's solution in a baby aged 6 months (fig. 21). The undoubted "intravenous" infusion of concentrated plasma, under pressure, into the saphenous vein, at the ankle, in infants with severe diarrhœa and vomiting, has ended in gangrene of the leg. Two such cases have been seen by M. Bodian and D. J. Waterson (personal communication). This is the subject of their particular study at the moment, the exact pathogenesis being as yet uncertain. Two cases have also been observed in infants where localised skin-patch gangrene, in the thigh and leg well above the

Digitized by Google

needle site, followed the infusion of plasma under pressure.

Wallace and Richards (1948) have noted also, in Army "practice" transfusions, the delayed development of ecchymotic areas in the arm well above the needle site. They suggest that it is due to intense spasm of the veins draining the biceps muscle, with rupture of some of the tributaries.

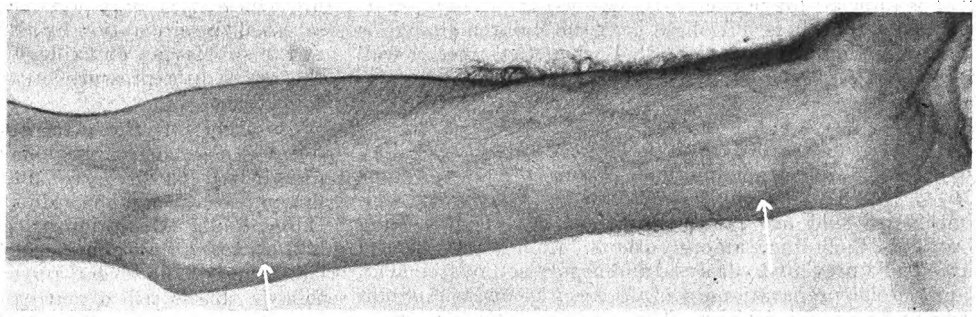


Fig. 24.—Ulnar artery subcutaneous near elbow and then proceeding below deep fascia. Vein-like appearance is shown; pulsation was evident only on close observation.

The segmental distribution of these skin patches is of particular interest in view of Wood Jones's (1948) comment that it is insufficiently appreciated that the limb has a number of self-contained functional venous units, and abundant arteriovenous communications in these areas to meet the circulatory emergency demands. It is probable—indeed to be expected—that such arteriovenous communications would be relatively larger in the infant and thus explain the retrograde filling, under pressure, of the arterial tree; certainly it is difficult to explain the intra-arterial thrombotic clot found in these "intravenous" tragedies in infants on any other basis.

ANATOMICAL VARIATIONS AT THE ELBOW

These can be best appreciated by a brief reference to embryological development. The limb buds are first pervaded by a capillary network; during the sixth week of fœtal life the primary arterial channels are laid down, and there is developed a main, or axial, artery which persists as the subclavian, axillary, and brachial arteries. In the forearm most of the axial artery undergoes suppression, and its primary course is represented by the branch of the interosseous artery accompanying the median nerve. "The radial artery arises at first at a higher level than the ulnar artery, but later establishes connexion with the main trunk near the site of origin of the ulnar, and the upper part of its original stem disappears" (Gray 1938).

Quain's (1844) careful study of 451 dissected arms provides a comprehensive account of the possible variations. High division of the brachial artery—i.e., above the elbow-joint—takes place in 1 out of 10 arms; and, contrary to the usual teaching, in only a third is such peculiarity bilateral. When the division is high, the ulnar artery almost invariably reaches the distal part of the arm by passing superficially to the flexor group of muscles (10% incidence). In its downward path it may hug the radial branch in the elbow area, but at times it takes a medial sweep to lie well apart (fig. 23). In its downward superficial course the ulnar artery may occupy one of three different positions: (1) subfascial all the way down (fig. 22); (2) subcutaneous in the elbow area and then below the deep fascia (fig. 24); or (3) subfascial in the upper part of the forearm, then subcutaneous, and in the distal third of the forearm subfascial again.

22

23

Fig. 22—Ulnar artery (arrow) in subfascial plane. High division of brachial artery is more usual finding when vessel pursues this course. (From Quain 1844.)

Fig. 23—Ulnar artery (arrow) passing down subcutaneously. Note high brachial origin and medial sweep at elbow.

When the ulnar artery pursues this superficial course, its volar interosseous branch comes off the radial division. This fact is of the utmost importance; for, if the brachial vessel divides high, retrograde injection into the aberrant ulnar branch is unlikely to reach the brachial artery, unless the circulation has been temporarily cut off. The interosseous branch, coming off the radial division, is therefore unlikely to suffer in any thiopentone thrombosis, and via this vessel the flushing and dilution of any ulnar injected thiopentone can continue. It is also to be noted that, when the course of the ulnar artery is superficial, the vessel is usually smaller, and compensatory enlargement is invariably found in the radial division. This will also enable the freer flushing of any irritants carried by the ulnar vessel. Such superficial ulnar vessels are derived from the vasa aberrantia and, like other superficial vessels, have a fuller nerve-supply than have the deeper branches, and are more readily thrown into spasm. The latter fact explains why, in cases 10 and 12, there has followed "immediate thrombosis and thickening" after injection of the superficial ulnar artery. The relationship of these vessels to the veins of the forearm are shown in figs. 25 and 26.

Arms have been examined to see if such abnormalities can be determined during life. The vulnerable superficial ulnar artery is often encountered. I. Jacobson, after a study of 200 arms of soldiers, informs me that in 25 the arteries near the antecubital fossa were in such a position that they could easily be inadvertently punctured when an injection was given (fig. 27). There were three abnormal superficial ulnar arteries in this group. At a small meeting where this was discussed, 4 out of 25 doctors present had subcutaneous ulnar arteries. Quain (1844) made this observation in the living subject.

Hyperextension of the elbow straightens the normal tortuosity of the brachial artery and fixes it for easier injection; this, therefore, requires particular care.

Pulsation in the normal young healthy person is not easily seen, and it is unjust criticism to comment that such thiopentone tragedies would not have happened if the anæsthetist had spent a few moments looking for these vessels. Lewis (1945) comments on the forearm vessels:

Digitized by Google

"It is unusual for normal arteries to show visible pulsation, and then it is but slight . . . the volume change is almost negligible and only noted when the arterial wall is pressed on."

PATHOLOGY

Thiopentone in 2·5% solution has a pH about 10·4–10·6 by the glass-electrode method (Tabin cited by Adams 1944). As Adams points out, the derivatives of thiobarbituric acid are rather unstable, the disintegration products including, among others, amides and acetyl urea. To prevent hydrolysis and separation of free acid, commercial preparations contain also, as buffer, sodium carbonate 6% by weight. Thiopentone is thus a strong alkaline irritant.

An artery, with its high muscle and elastic content, is obviously less distensible than the vein, and intra-arterial injection may thus be supposed to trap the thiopentone longer. Yet arteriography shows that a hypertonic solution (50% of diodone) rapidly injected passes through the limb within a few seconds. That period may, however, be sufficient for thiopentone to exert its action. Stretching of the arterial wall by rapid injection may be supposed to lead to arterial spasm and trapping of the solution. Arteriography, however, shows that any spasm of a major vessel produced by such stretch can be but momentary; for, if the needle is retained within the vessel and the injection repeated, the full anatomy of the tree is again reproduced. The radial artery is, however, an "irritable" vessel, and occasionally, after arteriography, may go into spasm, with loss of pulse for several hours, but with no ischæmic effects. Clinical experience shows that the superficial ulnar artery is similarly subject to spasm. The intra-arterial injection of thiopentone, except in the case of the ulnar arteries, was not followed by spasm of a major vessel, for the pulse continued at first in full volume.

Thrombosis was the essential pathological lesion; its onset was immediate in the ulnar-artery cases: in one evident after 50 min., in another within 6 hours, and in three it appeared to become complete on the eighth, tenth, and fifteenth day after the injection. Damage to the intima, due to puncture of the vessel, suggests itself, at first thought, as responsible for the thrombosis; but this does not follow arteriography, even when repeated, and when the intima can be presumed to have been scratched. Leriche (1945) reports a case where the femoral artery was punctured 30 times (with tourniquet on) for mercurochrome injections, with no subsequent local thrombosis. Suture of a vessel, including all its coats, is not followed by thrombosis, even in the non-heparinised patient. The small intra-arterial hæmatoma of the vessel wall does not alone cause spasm of a major vessel, as has been said to follow in the traumatic case (Cohen 1944). We can only conclude that the arterial intima appears to be particularly sensitive to thiopentone and solutions of high pH; for it tolerates extremely well hypertonic solutions used for arteriography and various therapeutic substances.

Damage to the intima is the precipitating factor, and microscopy indicates that an aggregation of platelets over the site of the damage forms the starting-point of thrombosis. Where late thrombosis has set in—eighth and tenth day (cases 9 and 11)—histological sections showed that the lumen may be lined with a thick layer of fibrin with a narrow channel through it (figs. 28 and 29); this means that even if the pulse is felt it gives no indication of the volume of blood-flow.

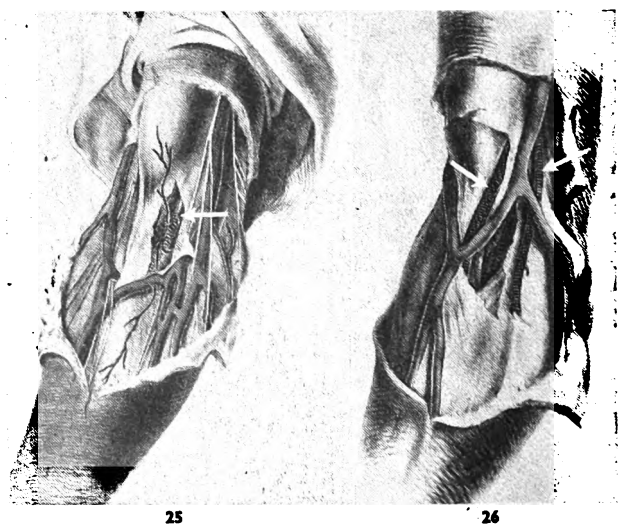
A thrombosis usually extends proximally no higher than the origin of the major collateral vessel next above the site of damage. As already remarked, the high thrombosis in these cases can only be explained by high ascent of the injected solution. This high injection against the flowing arterial stream, as arteriography and experiment indicate, is only possible if there has been temporary arrest of the circulation by clavicular or other compression of the subclavian or axillary artery, or failure to release the assistant's pressure or the rubber-band "venous" tourniquet.

Shunting of the drug into the skin has already been explained as responsible for the sloughing or discoloured patches of skin. The distal forearm and finger are affected according to the distribution of the thiopentone. Excretion of thiopentone into the muscles will lead to an outpouring of fluid, as with any irritating substance. The exact physico-chemical process which follows this is still a matter of argument, and Cameron (1946) has pointed out that we do not yet know whether it is due to the loosening of the cement substances binding cells together, or a physical alteration in the surface membrane lining the endothelial cells.

Where the vessels of supply to the muscles have completely thrombosed, muscle death has followed. The nerve ischæmia following thrombosis has also been shown to be responsible for the nerve effects. Where separate fingers have died, complete blockage of the digital vessels by thrombus has obviously been the cause; the clinical evidence of this is the fact that these fingers developed no œdema.

Where recovery took place, the digital vessels could only have been in spasm, and these fingers subsequently became œdematous. There is no evidence in man that continued spasm leads to arterial thrombosis.

We still have to explain why terminal gangrene of the finger-tips was a feature in several cases; for, as Lewis (1934) has shown in his studies on Raynaud's disease, the entire length of the digital artery is always affected in such spasm, and gangrene of the whole finger is to be expected. We cannot overlook the fact that in some of the cases the extent of finger gangrene corresponded to the area where Grant (1938) has shown the arterio-venous anastomoses to be most abundant. These anastomoses have thickened muscle walls and are known to be particularly well supplied with vasomotor nerves; they are maintained in a state of rhythmic contractility, which has a milking effect and adds impetus to the circulation on the venous side, which, in the fingers, has no "pumping" muscles to promote it. Clotting in the venous loop will thus be favoured, if intense spasm, due to the irritant, is maintained in these anastomoses. Animal experiment shows that during sleep and anæs-



25 26

Fig. 25—Superficial veins at elbow in relation to brachial artery (arrow).

Fig. 26—Arrangement of veins at elbow when brachial artery divides high: ulnar artery pursues, in this case, a subcutaneous course at first and pierces deep fascia. (From Quain 1844.)

Digitized by Google

thesia such anastomoses relax. Clinically also, cervical sympathetic block in one of the cases was followed by immediate vasodilatation, which suggests that the vessel is kept closed by a reflex whose efferent arc passes via the sympathetic ganglia. This observation needs confirmation; for, if true, it gives us a rational basis for the management of the finger gangrene.

The pathological material available to me has been in the main from thiopentone cases. Study of the tragedies following other drugs and therapeutic media indicate, however, that the circulation may be finally arrested by different mechanisms, several acting at the same time. These may be summarised as:

(1) Arterial thrombosis—most of the thiopentone cases.

(2) Arterial or distal arteriolar spasm.

(3) Extensive diffuse venous thrombosis, as after the accidental retrograde injection of sclerosants into the deep veins. I have seen diffuse venous thrombosis, in traumatic injuries, lead to limb gangrene, the arterial tree being patent and the major vessels not in agonal spasm.

(4) Extensive venous spasm. I have not seen gangrene per se follow this, but it may be a contributory cause of limb death. How great may be the peripheral resistance to arterial inflow in this type of spasm is well shown by Humble and Belyavin (1944); a pressure of 300 mm. Hg could not force the fluids into the veins.

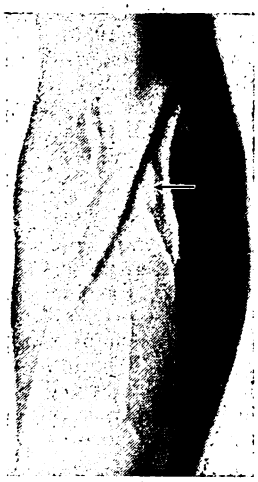


Fig. 27—Veins distended with rubber band. Arrow indicates superficial ulnar artery. Gliding of needle to enter median basilic vein may lead to puncture of artery.

(5) Mechanical blocking due to protein flocculation or drug precipitation, as in the concentrated plasma and myanesin cases.

(6) Arteriovenous communications enabling the retrograde spilling over of intravenous fluid into the arterial circuit. This is especially likely to happen if the fluid is given under pressure; it has been suggested as the possible explanation for leg gangrene following intravenous infusions in children.

There is need for experiments on animals to discover the pathological events; large animals are to be preferred, for in small animals such as the rabbit the vessels are too readily thrown into spasm by any handling and confuse the issue. Such facilities have not been available to me.

TREATMENT

Anticoagulants

It would require courage on the part of the anæsthetist to order the abandonment of the operation. Obviously that is the measure most desirable, for the formation of a thrombus indicates that there is urgent need for anticoagulant therapy—heparinisation of the patient. Such anticoagulant therapy may need to be long-continued, for the case-records indicate that thrombosis may come on as late as the eighth, tenth, or fifteenth day. To combat late thrombosis dicoumarin is best; its action, however, is delayed for 48 hours, and until then heparinisation must be continued. Such anticoagulant therapy may be inadvisable after some operations, but it is usually considered safe to start heparinisation after 2–3 hours; my experience is that, in the routine operation where adequate hæmostasis has been possible, heparin may be given even earlier. The early doses of heparin should be generous, for it will not be of much value to find at the end of, say, four hours that the clotting-time has not been raised, and that further heparin in increased dosage is necessary. I suggest in the adult 15,000 units at least as the initial dose.

This larger dosage is also important, for different batches seem to vary in their potency and in their "toxic" reaction (Brown 1946). Heparin is best administered as a saline drip into the tubing of which the nurse can inject the repeated doses (Medical Research Council 1944). Humble's cannula is a suitable alternative method for intermittent administration.

Fig. 28—Radial artery (case 9): intima thickened, and lumen filled with fibrin clot, leaving channel patent.

My experience is that intermittent administration is not adequate for the threatened arterial thrombosis; the clots form during the night ("free" period). Experimental studies (Kiesewetter and Shumacker 1948) confirm that a constantly prolonged coagulation-time is more desirable and superior, particularly as regards clotting in the smaller arteries.

If the anæsthetist feels certain that injection has been intra-arterial, it may be well worth inviting the surgeon to expose the vessel immediately and to inject heparin intra-arterially. Intra-arterial procaine, as first introduced by Goyanes in 1912, has been suggested, but its local action is evanescent unless a tourniquet is used; this could not be countenanced after thiopentone. Intra-arterial procaine has not been effective in the intense spasm that has followed the forgotten tourniquet and the crush injury (personal communications). Local injections of procaine round the artery were tried in two of the cases, with no effect; it has almost always failed to release spasm of a major vessel secondary to trauma.

Brachial-plexus Block

The anæsthetist should probably do a brachial-plexus block immediately. That should give the maximal vasodilatation in the hand and release the tone of the arteriovenous shunts on the fingers. I suggest brachial-plexus block rather than sympathetic block, because the anæsthetist is conversant with it, whereas sympathetic block, in my hands, is not so easy or so certain as the textbooks indicate. Brachial-plexus block will anæsthetise the vasoconstrictor fibres relayed from the sympathetic ganglia to the hand and forearm, the area which concerns us most; the periarterial sympathetic plexus supplying the upper portion of the brachial artery will not be affected, but this is not important. The forearm vessels will be affected, for it is now generally agreed that the vasoconstrictor nerves to the vessels leave the main nerve-trunks at short intervals to supply corresponding lengths of vessels. As Macintosh and Mushin (1944) have pointed out, brachial-plexus block is followed by some degree of Horner's syndrome in 50% of cases. That must indicate spread of the solution and blocking of the sympathetic ganglia, or its rami, as well.

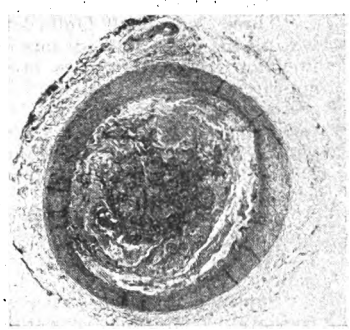


Fig. 29—Brachial artery (case 5): recent thrombosis and widespread superficial necrosis of intima.

Digitized by Google

Posterior sympathetic block is not without danger. In case 2 the lung was punctured in the heparinised patient, causing severe hæmoptysis. It is also easy to insert the needle into the dural sheath along the nerve-trunks and to inject the fluid into the spinal canal. I am aware of several tragedies which have not been recorded. Cyriax (1937) in a report on observations made at Leriche's clinic, reported one such collapse; this followed what was believed to be accidental injection into the vertebral artery. Mackey and Scott (1938), discussing the infiltration of the stellate ganglion in apoplexy, describe a case where immediate respiratory paralysis, lasting 30 min., followed such injection "into the vein." Arnulf (1947), in a book on stellate-ganglion block, describes several such tragedies and alarming incidents, which he, however, regards as "exceptional."

The march of events is well shown in a note sent to me by an anæsthetist who tried sympathetic block in one of the thiopentone cases:

"The patient lying prone, a needle was inserted $2^1/_2$ finger-breadths lateral to the space between the spines of C7 and T1. The patient complained of paræsthesia in the arm; and, after tests for the aspiration of blood and cerebrospinal fluid, 15 ml. of 1% procaine, without adrenaline, was slowly injected.

"There was some complaint of pain in the arm during the injection and, at the end of this, of nausea. He was turned on to his back and found to be unconscious. Respiration ceased, the pulse deteriorated and disappeared. Nikethamide 1·5 ml. was injected intravenously, artificial respiration begun, and oxygen and carbon dioxide administered.

"Patient's condition being grave, the surgeon injected 1·5 ml. of nikethamide into the heart. Almost at once the pulse returned, very full and rapid, and a further 1·5 ml. was given intramuscularly. The time between the cessation of the heart and recovery was $1^1/_2$–2 min.

"Respiration did not return, and artificial respiration was continued. While this was proceeding, patient's pupils, which had been large and eccentric, became smaller, there were roving eye movements, and his facial muscles above the mouth began to twitch. It was 20–25 min. before respiration restarted, and during this time artificial respiration was continued.

"Movements of the mouth and face now became more pronounced, and there was also cyclical twisting of the head from side to side. The legs were spastic, no jerks could be elicited, and plantar reflexes were absent.

"About 15 min. after the restart of respiration, the picture was that of a cerebral catastrophe; patient's movements became more pronounced, and he was soon throwing himself about the bed most violently, groaning and coughing, with his facial and neck muscles moving. Sedation being imperative, morphine was given.

"Three and a half hours later he was quieter but still tossing his head and unconscious. Four hours after the injection he was far more tranquil and, when spoken to, appeared to understand but could not talk or indicate by gesture that he understood. He now reacted for the first time to painful stimuli—i.e., turned his face away from a pinprick. The legs had become flaccid. The right plantar response, which had been extensor, was now flexor; the left still dubious.

"Seven hours after the injection he was awake, answered questions normally, and complained only of a little nausea. The legs were of normal tone, with the left leg possibly slightly more spastic.

"Subsequent convalescence was complicated by auricular fibrillation (confirmed by cardiologist). A week after the original injection the pulse rhythm had returned to normal."

The brachial-plexus block should probably be repeated at the end of the operation, for a report on one of the cases indicated that its effect lasted less than 4 hours. Amethocaine, because of its long-continued action, should form part of the anæsthetic solution. Brachial-plexus block cannot be repeated after heparinisation, for should the subclavian artery be pierced—always a minor hazard with this procedure—serious hæmorrhage might follow.

General Anæsthesia

Should the operation have to continue, the choice of anæsthetic is important. General anæsthesia removes vasomotor tone from peripheral blood-vessels as effectively as does blocking of sympathetic nerves (Abramson 1944). Such peripheral vasodilatation should theoretically cause a steep fall in blood-pressure, and there is a rise of sympathetic tonus in other regions, such as the great splanchnic area, which compensates and maintains the normal level (White 1935). Craig et al. (1932), investigating the thermal changes in the limbs during full anæsthesia, found a rapid rise of temperature in the skin of the hand, with no additional increase on nerve-block, indicating complete release of sympathetic tone. Scott and Morton (1930) showed that with nitrous oxide there may be vasoconstriction during the period of struggle, and it is thus not a suitable anæsthetic for these cases. Cyclopropane has, as regards the circulation, some advantages. Waters (1936) has shown that in anæsthetic concentration it relaxes the peripheral blood-vessels, and Abramson et al. (1941) showed that there was quadruple maximal increase in flow almost immediately after the cyclopropane anæsthesia was begun. Deep anæsthesia is not, however, desirable; for, according to experimental work by Mann et al. (1935), the increase in blood-flow in the peripheral arteries, as measured by thermostromuhr, falls to less than 20% with deep anæsthesia, as compared with the 64% rise with light surgical anæsthesia. The fall of general blood-pressure with deep anæsthesia will affect the blood-flow through the limb.

Morphine and Sleep

Adequate quantities of morphine are required to relieve pain—Goetz (1943) and Wilkins et al. (1938) have shown that painful stimuli will cause intense peripheral vasoconstriction—and to relax vessel spasm (Learmonth 1946). Sleep inhibits vasoconstrictor tone, and during sleep, in the normal person, full peripheral vasodilatation is obtained. This has been confirmed by taking thermocouple leads from the toes (Ingram 1936).

Forcing the Collateral Circulation

The patient should be kept warm and an attempt made to force the collateral circulation by immersion of opposite limbs in hot water (110°F) or by using a hot cradle over the rest of the body. The warmed blood returning from these limbs to the thalamus inhibits the vasoconstrictor tone of the vasomotor centre and leads to dilatation of the peripheral vessels; blood-flow to the fingers, in a normal person, may thus be increased 100 times. Such treatment, however, has not been successful in these thiopentone cases; nor has it in the intense digital spasm due to high-altitude frostbite. Warming the body will sometimes not release the spasm in some of the Raynaud's attacks following cold.

Elevation of Limb

The affected limb should be kept elevated to assist both venous and lymphatic flow. Such elevation should not, however, be above heart level, and the effect on pain should be observed. "The customer is right" is a sound rule: if the patient complains of excessive pain, the limb should be slightly lowered (Cohen 1946a). A point often overlooked, and I have seen it in one of the thiopentone cases, is that, if the patient is permitted to sit up, the pillows must be adjusted to raise the arm to shoulder level (Barnes 1942).

The importance of promoting venous flow cannot be over-emphasised, for experience shows that, should venous clotting take place in the limb with sluggish circulation, the fate of the limb will be sealed (Cohen 1946b, Leriche 1945). Gentle finger exercises may be encouraged, but vigorous movement should not be permitted, for such exercise may precipitate the further

Digitized by Google

spread of thrombosis. It is believed that the arterial pulsation plays a not inconsiderable part in driving blood along the accompanying vein (Clark 1939); since the thrombosis is so extensive, elevation will compensate for this lack of pulsation.

The importance of assisting the lymphatic drainage by elevation, to cope with the œdema of hand and forearm in these cases, must also not be overlooked. Courtice (1946) in studies of chemical warfare, and Drinker and Yoffey (1941), in studies of burns, have shown, by cannulating the lymphatics experimentally, how great may be the return of lost fluid via this circulation.

Temperature of Limb

The limb should be wrapped in a sterile towel and covered with wool; it should not be kept cool or exposed to the air. Such cooling increases arterial vasoconstriction, and the veins and venules contract as a direct response to cold. Prevention of heat-loss from the limb is important; as the oxyhæmoglobin dissociation-curve shows, oxygen is poorly released at lower temperatures. With mild warmth, venous tone is diminished and arterial pressure is transferred to the venous side more completely than when tone is high (Bowers et al. 1945). Excessive heating of the limb with a cradle or by other means must, however, be avoided, for it is well known that the metabolism of the cells is thus stepped up, increasing their oxygen demands. Pochin (1943) has shown that, if the blood-supply to a rabbit's ear is obstructed by placing a wooden plug in the external ear and binding this with wide elastic tubing, œdema subsequently develops on release of the circulation; the extent of gangrene that develops in the ear will depend not on the amount of œdema but on the temperature of the room in which the rabbit is allowed to recover. In a warm room (88°F) gangrene is a common sequel, though the œdema may be no greater.

Vasodilators

Papaverine, alcohol, aspirin, and other anti-spasmodics have been used in these thiopentone cases with no dramatic improvement. Such measures may be tried; but it is well to note that Davis et al. (1943), after experiments on both normal persons and patients who had recovered from injuries to fingers following severe cold, concluded that "contrary to the general accepted action, as reported in textbooks, none of these drugs (amyl nitrite, nitroglycerin, alcohol) cause any elevation of the temperature in the distal parts or dilatation of the capillary loops."

Experimentally, Laufman and Method (1947) have shown papaverine hydrochloride to be effective in releasing the residual vasospasm following gut strangulation; it is thus reasonable to use it. Intravenous ether 2·5% in 5% glucose—1 litre dosage—may also be tried.

Surgical Measures

When immediate exploration has not been done, the limb needs most careful watching—as if it were an acute intestinal obstruction—and the decision about exploration must be made within six hours. If operation is decided on, and the patient is already heparinised, an interval of two or three hours is necessary; but the use of protamine as a direct antidote to heparin, or a blood-transfusion, may allow earlier operation; the clotting-time will be a guide. The operation of choice is probably incision of the vessel and extraction of the clot. The vessel should preferably be opened well proximal to the injection site, so that the ultimate suture line of the vessel will not lie within the damaged area. The clot may be extracted with forceps or by aspiration. Experience with emergency embolectomies indicates that, if exploration is not early, the clot is adherent to the vessel wall and suction cannot aspirate it. I have had occasion, in this type of case, to incise the vessel in two of the distal branches and remove the clot by proximal syringing and flushing. This may be a useful expedient in some of the thiopentone cases. A distal intra-arterial injection of heparin should always be given at the time of the operation. After such manipulation of the vessel suture may be difficult, and the attempt to remove the clot may have mutilated the suture line. The operator may be tempted to tie the vessel; but it should be borne in mind that a glass cannula will allow the stream to continue if the patient is heparinised. The cannula may be removed three days later, and will, in the meantime, have given a good stream down and prevented clotting on the damaged intima (Mustard 1946, Cohen 1946b).

I am by no means certain of the value of immediate arteriotomy. The results after brachial embolectomy have caused some dissatisfaction, and opinion in this country no longer whole-heartedly favours it. B. G. Maybury (personal communication) declares, "the best treatment for a brachial embolus is sympathectomy." It may therefore be sufficient to heparinise the patient and try to achieve "medical" sympathectomy by measures such as reflex heating and tetraethyl ammonium chloride. The latter is said to have a selective autonomic block action in 500 mg. dosage (Ballantine 1947), and a well-marked increase in peripheral blood-flow is obtained, despite the generalised vasodilating effect. The associated well-marked fall of blood-pressure is the obvious disadvantage.

Arterectomy (excision of a segment of the vessel as practised in some of the cases, has to my mind no advantage; excision of the entire bifurcation ("triple ligation") usually ends disastrously and should be avoided (Maybury 1946). There is no evidence for the theoretical view that clotting in a vessel holds the collaterals in "reflex spasm" and that arterectomy will release such spasm (Cohen 1944, Lewis 1943).

Late surgical intervention does not seem worth while; all the cases in which late exploration was done fared badly. In view of the extensive thrombosis, operation could only prove of value if a full flushing by multiple arteriotomies and subsequent heparinisation of the patient could be practised. There is as yet no clinical experience for this; and, since microscopical sections show that the intima is severely and extensively damaged, further clotting is likely to take place. In children especially such late operations seem inadvisable. Gross (1945), who has made a close study of embolic infarction in children, emphasises that "occlusion of the large artery in the child at first seems incompatible with the survival of the limb"; yet it is remarkable what a first-class result conservative measures produce.

PROPHYLAXIS

Various suggestions have been made, of which most anæsthetists are aware: spending a moment and palpating and looking for arterial pulsation (Minnitt and Gillies 1944); the selection of a vein outside the cubital fossa or, even better, the almost constant vein over the dorsal and lateral aspect of the radius; and injection of a small quantity of thiopentone and waiting to see if the patient develops pain or not. A knowledge of the abnormalities of the arterial tree on the front of the elbow-joint is now a sine qua non to the anæsthetist. Avoidance of vigorous extension of the elbow, seeing that the venous tourniquet is not too tight, and the insistence on a good light are additional necessary precautions. "An emergency prepared for ceases to be an emergency" is a maxim that might well be engraved on the thiopentone ampoule.

SUMMARY

Eight unrecorded cases of catastrophic results following the inadvertent intra-arterial injection of thiopentone are described; five of these subsequently ended in forearm or arm amputations.

Digitized by Google

Four previously published cases are reviewed; in three of these full operation details and some pathological material have enabled a closer study.

Experience gained from arteriography is used to shed light on factors such as pain on arterial puncture, vessel spasm after injection, and the height that injected fluid will ascend against the flowing arterial stream.

Phlebography indicates that there is considerable distal blood-flow in the forearm when an injection is given at elbow level; the effects and dangers of venous thrombosis are emphasised.

Arteriography and experiments confirm that, to explain the high thrombosis and skin lesions in some of the cases, there must have been temporary occlusion of arterial flow during the injection, either by inadequate release of the tourniquet or by posture of the patient on the operating-table. The mechanical factors likely to obstruct arterial flow at the cervical outlet are described.

Clinical features are discussed: the character of the pain; sloughing cutaneous patches due to thiopentone shunt into the cutaneous arteries; muscle death due to arterial thrombosis; œdema of forearm; nerve effects due to interference with the blood-supply of the main trunks; and late thrombosis.

The effects of thiopentone are held to be due to its high pH. Trapping of the solution in the arterial tree is regarded as momentary, for with small dosage used in some of the cases unconsciousness was only a little delayed.

Extensive thrombosis of the major vessel, and distal arteriolar spasm, are shown to be in the main responsible for the sequelæ. Other mechanisms are discussed.

The variable anatomy of the arterial tree at the elbow is described, and the less serious lesion, following injection into an aberrant ulnar vessel, is shown to be due to the arrangement of the divisions of the brachial artery.

The rationale of the management of these cases is described. Brachial-plexus block is advocated as part of the therapy, and posterior sympathetic block regarded as difficult and hazardous.

If operation has to continue, the most suitable anæsthetic as regards the peripheral vessels is cyclopropane.

Anticoagulant therapy (heparin), in large doses early, is advocated, with exposure and direct injection into the brachial artery, if the anæsthetist is sure of the accident.

Arteriotomy and extraction of clot are probably the operation of choice, the incision being made well above the injection site.

Arterectomy has no physiological sanction and is particularly dangerous if triple ligation is undertaken.

Late exploration is regarded as not worth while.

The local care of the limb is detailed.

Tragedies that have followed the intra-arterial injection of contrast media or therapeutic substances have been collected.

Intra-arterial thiopentone may be hazardous to life as well as to limb.

These cases are in need of intensive study, for they throw much light on the pathological events in the ischæmic limb.

The buffering of thiopentone to render it non-irritating seems within the ken of pharmacologists.

There is urgent need for further experimental work, using larger animals.

These tragedies carry bitter memories for most of the anæsthetists responsible. I have therefore thought it advisable to suppress their names and can merely acknowledge their courtesy and great help in making available to me all the details. To the surgeons who have given me the right to publish their operative findings, and even to criticise from the "touch-line," I can only offer similar anonymous expression of my gratitude; it was felt better for me not to indicate, by naming the surgeons, where such tragedies took place. Human nature, being what it is, is apt to blame and see the faults in others only too readily.

Prof. J. Dible has kindly given me his opinion on the vessel sections. Prof. J. Kirk, of Middlesex Hospital, has acted in most stimulating fashion as the "backroom boy," discussing with me the variable anatomy of the arterial tree and making available some of Quain's original masterpieces. It is a pleasure to acknowledge the cheerful coöperative expert help of Mr. V. W. Willmott, A.R.P.S., of the British Postgraduate Medical School, in preparing the photomicrographs and other photographs for me. I am much indebted to Mr. J. Robson for the illustrations.

REFERENCES

Abramson, D. I. (1944) Vascular Responses in the Extremities of Man in Health and Disease. Chicago; p. 222.
— Grollman, A. I., Schwartz, A. L. (1941) *Anesthesiology*, **2**, 186.
Adams, R. C. (1944) Intravenous Anesthesia. New York.
Adams, W. E. (1942) *J. Anat.* **76**, 323.
Albert, M., Mitchell, W. R. D. (1943) *Lancet*, **i**, 519.
Arnulf, G. (1947) L'infiltration stellaire. Paris; p. 38.
Ballantine, H. T. (1947) *Ann. Surg.* **126**, 873.
Barcroft, H., Edholm, O. G. (1946) *Lancet*, **ii**, 513.
Barnes, J. M. (1942) *Ibid*, **i**, 531.
Bentley, F. H., Schlapp, W. (1943) *J. Physiol.* **102**, 62.
Bowden, R. E. M., Gutmann, E. (1945) *Lancet*, **ii**, 768.
Bowers, E., Campbell, E. J. M., Johnston, C. H. P. (1945) *Ibid*, **i**, 460.
Brown, J. J. M. (1946) *Proc. R. Soc. Med.* **39**, 483.
Bywaters, E. G. L., Stead, J. K. (1945) *Clin. Sci.* **5**, 195.
Cameron, G. R. (1946) *Proc. R. Soc. Med.* **40**, 1.
Clark, W. E. Le G. (1939) The Tissues of the Body. London; p. 170.
Cohen, S. M. (1944) *Lancet*, **i**, 1.
— (1946a) *Guy's Hosp. Gaz.* **60**, 80.
— (1946b) *Proc. R. Soc. Med.* **39**, 718.
Courtice, F. C. (1946) *J. Physiol.* **104**, 321.
Craig, W. M., Horton, B. T., Sheard, C. (1932) *Proc. Mayo Clin.* **7**, 537.
Cyriax, J. H. (1937) *Brit. med. J.* **ii**, 1199.
Davis, L., Scarff, J. E., Rogers, N., Dickinson, M. (1943) *Surg. Gynec. Obstet.*, **77**, 561.
Dos Santos, R. (1935) *Bull. Soc. nat. Chir.* **61**, 585.
Drinker, C. K., Yoffey, J. M. (1941) Lymphatics, Lymph, and Lymphoid Tissue. London.
Erb, W. H. (1944) *Delaware St. med. J.* **16**, 147.
Evans, F. (1939) *Lancet*, **ii**, 252.
Fontaine, R., Forster, E. (1946) *Lyon chir.* **41**, 173.
Foote, R. R. (1945) *Lancet*, **ii**, 690.
Freudenthal, W. (1924) *Arch. Derm. Syph., Wien*, **147**, 155.
Gammel, J. A. (1927) *J. Amer. med. Ass.* **88**, 998.
Gillis, L. (1945) *Brit. med. J.* **ii**, 686.
Goetz, R. H. (1943) *S. Afr. J. med. Sci.* **8**, 65.
— (1946) *Amer. Heart J.* **31**, 146.
Grant, R. T. (1938) *Clin. Sci*, **3**, 157.
Gray, H. (1938) Anatomy. London; p. 150.
Griffiths, D. L. (1940) *Brit. J. Surg.* **28**, 239.
Gross, R. E. (1945) *Amer. J. Dis. Child.* **70**, 61.
Guthkelch, A. N. (1943) *Brit. med. J.* **ii**, 245.
Hasler, J. K. (1948) *Proc. R. Soc. Med.* **41**, 133.
Hewspear, D. (1945) *Lancet*, **i**, 116.
Hoenigsberger, F. (1943) *Ibid*, **ii**, 14.
Holmes, W., Highet, W. B., Seddon, H. J. (1944) *Brit. J. Surg.* **32**, 259.
Humble, J. G., Belyavin, G. (1944) *Lancet*, **ii**, 534.
Hunter, A. R. (1943) *Ibid*, **i**, 46.
— (1947) *Brit. med. J.* **i**, 43.
Ingram, P. W. (1936) *Edinb. med. J.* **43**, 672.
Johnson, B. (1946) *Guy's Hosp. Gaz.* **60**, 336.
Jones, F. W. (1948) *Lancet*, **i**, 165.
Kiesewetter, W. B., Shumacker, H. B. jun. (1948) *Surg. Gynec. Obstet.* **86**, 687.
Lambret, O. (1935) *Bull. Soc. nat. Chir.* **61**, 173.
Laufman, H., Method, H. (1947) *Surg. Gynec. Obstet.* **85**, 675.
Learmonth, J. R. (1946) *Proc. R. Soc. Med.* **39**, 488.
Leclerc, G. (1935) *Bull. Soc. nat. Chir.* **61**, 180.
Lees, J. (1943) *Lancet*, **i**, 788.
Leo, E. (1937) *G. ital. Clin. trop.* **1**, 297 (see *Trop. Dis. Bull.* 1938, **35**, 262).
Leriche, R. (1945) *Lyon chir.* **40**, 417.
Leveuf, J. (1935) *Bull. Soc. nat. Chir.* **61**, 6.
— (1938) *J. Chir., Paris*, **51**, 177.
Levin, A., McElroy, D. M. (1944) *Brit. J. Surg.* **31**, 240.
Lewis, Sir T. (1934) Clinical Science Illustrated by Personal Experiences. London; p. 143.
— (1936) Vascular Disorders of the Limbs. London.
— (1942) Pain. New York.
— (1943) *Proc. R. Soc. Med.* **36**, 522.
— (1945) Exercises in Human Physiology. London; p. 1.
— Pickering, G. W., Rothschild, P. (1931) *Heart*, **16**, 1.
Luke, J. C., Miller, G. G. (1948) *Ann. Surg.* **127**, 426.
Lundy, J. S. (1942) Clinical Anæsthesia. London; p. 542.
Macintosh, R. R., Heyworth, P. S. A. (1943) *Lancet*, **ii**, 571.
— Mushin, W. W. (1944) Local Anæsthesia: Brachial Plexus. London.
Mackey, W. A., Scott, L. D. W. (1938) *Brit. med. J.* **ii**, 1.
Mann, F. C., Essex, H. E., Herrick, J. F., Baldes, E. J. (1935) *West. J. Surg.* **43**, 177.
Maybury, B. C. (1946) *Proc. R. Soc. Med.* **39**, 493.
Medical Defence Union (1947) Report for 1946, p. 17.
Medical Research Council (1944) Arterial Injuries. London.
Minnitt, R. J., Gillies, J. (1944) Textbook of Anæsthetics. Edinburgh.
Mustard, W. T. (1946) *Ann. Surg.* **124**, 46.
Ogilvie, T. A., Penfold, J. B., Clendon, D. R. T. (1948) *Lancet*, **i**, 947.
Okada, E. (1905) cited by Adams (1942).
Parkes, A. R. (1945) *Brit. J. Surg.* **32**, 403.

Continued at foot of next page

Digitized by Google

ACUTE TRANSVERSE MYELITIS COMPLICATING PNEUMONIA

REPORT OF A CASE

A. I. SUCHETT-KAYE
M.D. Paris
ASSISTANT MEDICAL OFFICER, ST. CHARLES' HOSPITAL, L.C.C.

MYELITIS, though common in many different infections, is rarely a complication of pneumonia. Hassin and Broder[1] reported a case in which the patient died despite treatment with sulphonamides and penicillin, and necropsy showed bronchopneumonia of the right lower lobe and extreme softening of a dorsal segment of the spinal cord. Sheppe et al.[2] recorded the history of a naval officer who, during an attack of primary atypical pneumonia, developed an acute myelitis with paraplegia, paralysis of the intercostal muscles, and typical changes in the cerebrospinal fluid (C.S.F.); he subsequently recovered without sequelæ.

The following case of pneumonia ended fatally because of the onset of a severe transverse myelitis.

A lorry driver, aged 40, was admitted to St. Charles' Hospital on April 17, 1947, with seven days' history of dyspnœa, cough, hæmoptysis, and pain in the left side of his chest.

On admission his temperature was not raised, but his respirations and pulse were rapid. A cough producing copious sticky heavily bloodstained sputum was present. The percussion note was impaired at the left base, with diminished air entry and moist crepitations. The abnormal physical signs became more pronounced next day, and the patient's general condition deteriorated. He looked pale, thin, and toxic; his tongue was dry and coated; and though his temperature was still normal his pulse-rate was 100–140 per min. All other systems appeared to be normal. No tubercle bacilli were found on repeated examinations of the sputum, but one specimen grew predominantly Pfeiffer's bacillus. Pneumonic consolidation of the left lower lobe was diagnosed, and 'Sulphamezathine' was given in full doses. After three days the hæmoptysis stopped, and a chest radiogram now showed enlargement of the left hilar lymph-glands and patchy consolidation in the left lower lobe. A blood-count soon after admission revealed a leucocytosis of 23,000 white cells per c.mm. (polymorphs 81%, lymphocytes 17%, eosinophils 1%, monocytes 1%). The urine was normal.

On April 21 the patient complained of numbness and tingling in both legs. He could not micturate voluntarily, and his bladder became much distended. Voluntary power was diminished in the legs, with patchy loss of all forms of sensation over the lower limbs and trunk. The tendon-reflexes were normal and the plantar response flexor on both sides. Next day, for the first time since his admission, the patient's temperature rose to 101°F, while his pulse-rate remained at 120–140 per min. Blood-pressure 150/100 mm. Hg. An acute transverse myelitis was now obviously present: there was a complete flaccid paralysis with loss of all sensation up to the level of C6, with paralysis of the urinary and rectal sphincters and the intercostal and other respiratory muscles. Respiratory distress was pronounced and it w aggravated by the consolidation of lung.

On April 22 the C.S.F. was slightly turbid; pressure 200 mm. Hg; Queckenstedt test negative; contained 220 white cells per c.mm., with slightly more lymphocytes than polymorphs, and 150 red cells per c.mm.: globulin increased; total protein 320 mg. per 100 ml.; chlorides 680 mg. per 100 ml.; gram film showed pus cells but no organisms; no tubercle bacilli were found in Ziehl-Neelsen film; culture sterile; colloidal gold test 5554223210; Wassermann reaction negative.

In a few hours the patient's dyspnœa became alarming, with shallow and laboured respiration, cyanosis, and inability to expectorate. The sulphonamide treatment was supplemented with penicillin, and the patient was placed in a mechanical respirator. There were no signs of improvement however; his fever became hectic in type (99–104°F) and the consolidation spread to the whole left lung. Throughout the illness the spinal-cord lesion showed no change, the level of sensory loss remaining about constant. The patient's general condition occasionally improved temporarily, but the persistence of the paraplegia and pyrexia were of sombre prognosis. The C.S.F. unexpectedly became normal. On April 25 it was still slightly opalescent; pressure 150 mm. Hg; Queckenstedt test negative; white cells 82 per c.mm., lymphocytes greatly predominating; total protein 40 mg. per 100 ml.; globulin only a trace; chlorides 670 mg. per 100 ml.; no tubercle bacilli seen in stained film; cultures sterile. By April 30 it was clear and "water-white"; pressure 150 mm. Hg; 12 lymphocytes per c.mm.; total protein 20 mg. per 100 ml.; globulin not increased. Repeated blood-cultures were sterile; Wassermann reaction and Kahn test were negative; radiography of the cervical spine showed no abnormality.

The patient died on May 15, after remaining in Drinker's apparatus for 23 days, during which time he had two courses of sulphonamides (total 64 g.) and of penicillin (total 17,100,000 units).

Necropsy (Dr. C. E. Bryson).—Unresolved pneumonia of left lung involving both lobes; early abscess formation; right lung emphysematous and purulent bronchitis present. Bladder contained some turbid urine but there was no actual cystitis (a fact worth mentioning considering the number of times the bladder had to be catheterised during life). The mid-cervical cord (C4–D3) was œdematous and very soft, with disorganisation of the grey matter, consistent with an acute transverse myelitis: the central canal was dilated in one segment at the level of C7. Tissues of segments C5, C6, and D1 examined histologically confirmed the diagnosis of acute myelitis.

DISCUSSION

In this case an otherwise ordinary pneumonic consolidation in an afebrile patient, with signs of toxæmia, became complicated by a transverse myelitis affecting predominantly the cervical segments. From the beginning the patient, though relatively young, showed little natural resistanee to the illness. The paralysis of respiratory muscles, necessitating the continuous use of the iron lung, was an important factor in aggravating the pneumonic process, and the patient finally died of asphyxia.

At no time did the injured spinal cord show any clinical evidence of recovery, though the acute inflammation, as judged by the C.S.F., may eventually have subsided. The severe hæmoptysis and paraplegia at first suggested tuberculosis, especially since the C.S.F. showed lymphocytic predominance with absence of organisms. It seems probable, however, that both the pneumonia and the myelitis were caused by the same virus. This would explain the initial consolidation without pyrexia, the absence of crisis and response to chemotherapy, and the failure to isolate a causative organism in the sputum.

I am indebted to Dr. A. J. H. Reford for his help in the management of the case.

1. Hassin, G. B., Broder, S. B. *J. Neuropath. exp. Neurol.* 1946, 5, 106.
2. Sheppe, W. M., Osterman, A. L., Ahroon, C. R., Zuflacht, J. J. *J. Amer. med. Ass.* 1943, 122, 1245.

MR. COHEN: REFERENCES—*continued*

Payne, R. T. (1939) *Lancet*, i, 816.
Pochin, E. E. (1943) *Clin. Sci.* 4, 341.
Porritt, A. E., Debenham, R. K., Ross, C. C. (1945) *Brit. med. J.* ii, 377.
Prendergrass, E. P., Chamberlin, G. W., Godfrey, E. W., Burdick, E. D. (1942) *Amer. J. Roentgenol.* 48, 741.
Quain, R. (1844) The Anatomy of the Arteries of the Human Body. London.
Roberts, N. (1942) *Lancet*, ii, 498.
Samuels, S. S. (1945) Diagnosis and Treatment of Diseases of the Peripheral Arteries. London; p. 165.
Schmuttermayer, F. (1936) *Wien. klin. Wschr.* 49, 1197 (see *Trop. Dis. Bull.* 1937, 34, 65).
Scott, W. J. M., Morton, J. J. (1930) *Proc. Soc. exp. Biol., N.Y.* 27, 945.
Solomons, B. (1945) *Brit. med. J.* i, 592.
Van der Post, C. W. H. (1942) *S. Afr. med. J.* 16, 182.
Wagner, F. B. jun. (1944) *J. Amer. med. Ass.* 125, 958.
Wallace, J., Richards, R. D. (1948) *Brit. med. J.* i, 640.
Walsh, E. N., Wyatt, J. L. (1945) *J. Amer. med. Ass.* 129, 1255.
Waters, R. M. (1936) *Brit. med. J.* ii, 1013.
White, J. C. (1935) The Autonomic Nervous System. New York.
Wilkins, R. W., Doupe, J., Newman, H. W. (1938) *Clin. Sci.* 3, 403.
Wright, H. P. (1947) *Proc. R. Soc. Med.* 40, 197.
Wright, I. S. (1945) *Amer. Heart J.* 29, 1.

Digitized by Google

Reviews of Books

British Surgical Practice

Vol. III. Editors: Sir ERNEST ROCK CARLING, F.R.C.S., F.R.C.P., consulting surgeon, Westminster Hospital; J. PATERSON ROSS, M.S., F.R.C.S., director of surgical clinical unit, St. Bartholomew's Hospital, and professor of surgery in the University of London. London: Butterworth. 1948. Pp. 561. 60*s*.

WE have already reviewed the first two volumes of *British Surgical Practice*.[1] Volume III is no disappointment. It contains 63 sections, beginning with "Cæsarean Section" and closing, appropriately, with the "Eyelids." The ear, the eye, and endoscopy account between them for 28 sections. Some of the articles are better than others, but there is not a bad article in the book. The uniform lucidity of contributions by more than 50 authors is a great tribute to the editors, and the illustrations are numerous and good. It is clear, as the successive volumes emerge, that this work is achieving the very difficult and ambitious task which it set out to accomplish—to present an up-to-date and authoritative survey of British surgery.

Diagnostic Procedures in Virus and Rickettsial Diseases

Editor: T. FRANCIS, jun. New York: American Public Health Association. 1948. Pp. 352. $4.

To diagnose most of the virus diseases described in this book, inoculation of animals is needed on a scale practicable in this country only in the better equipped research institutes. To diagnose others, however, much may be done by the use of fertile eggs and by various in-vitro tests. The authors of the chapters in this book are all experts and describe in great detail methods of working with their own special viruses—methods which will often not be possible except to specialists. The transmission of mumps to monkeys, or of sand-fly fever to human volunteers, for instance, are never likely to be counted regular "diagnostic procedures." The precautions necessary to avoid infecting laboratory staff are described, and some instructions are offered on the proper care of laboratory animals. The account of psittacosis by Meyer and Eddie is particularly good. That by Rake on lymphogranuloma venereum inflicts on us an unaccustomed binomial nomenclature: we are asked to call the virus *Miyagawanella lymphogranulomatosis* (it seems unlikely that many of us will). Parker's chapter on variola and vaccinia is less full than most, and does not mention hæmagglutination. That by Feller on primary atypical pneumonia tells much about cold agglutinins and agglutination of the MG streptococcus—both far from being pathognomonic tests—but little about the virus described by Eaton and his colleagues. But most chapters—on mumps, poliomyelitis, encephalitis, herpes simplex, and so on—are very good. The writers are highly individual, and there is some overlapping and perhaps even a little contradiction in the accounts by different authors of similar techniques; but the book is a valuable reference work for those engaged in research and in public health.

Calcium and Phosphorus in Foods and Nutrition

HENRY C. SHERMAN, Mitchell professor emeritus of chemistry, Columbia University. New York: Columbia University Press. London: Oxford University Press. 1947. Pp. 176. 15*s*.

MUCH work has been done on calcium and phosphorus metabolism since Professor Sherman wrote the first edition of his *Chemistry of Food and Nutrition*; and few have so good a claim to bring the subject up to date in a book with a fairly general appeal. He begins by explaining why there is a nutritional problem connected with calcium and phosphorus: the animal is born with so little and needs so much that food which is otherwise satisfactory may fail to meet the body's requirements. There follows a general account of the calcium in the body, its combined forms, and its functions in the bones and tissues, which leads to an excellent study of the effects of food and growth on the body's calcium content. He deals well with the vexed question of calcium and phosphorus requirements and the problems of minimal and optimal intakes, but is not so happy when discussing why some foods supply calcium more readily than others.

Professor Sherman is at his best when dealing with the relationship between intake and retention, pointing out that passably normal health can be maintained—for a lifetime and even through successive generations—on very different levels of calcium intake and output, and on somewhat different concentrations of calcium within the body. He then marshals evidence to show that a high intake of calcium is always beneficial, even in elderly people, and that 1 g. a day is a good all round figure, with rather more for adolescents and for pregnant and nursing women. In his view, an excess, within reason, has no pathological consequences, but not everybody who believes this has the courage to say so, as many will recall from the controversy that arose here over the addition of calcium to flour.

There are a few weak points in the book; Professor Sherman implies that phosphorus deficiencies are not uncommon in infancy, which seems improbable, and his ideas about rickets may be applicable to the rat but can scarcely be accepted as applying to man. There are a few serious mistakes (adenine is numbered among the pyrimidines rather than the purines) and some omissions which workers in this country will find difficult to excuse. Thus the rôle of phytic acid in calcium metabolism and its importance in cereal diets are not discussed, though quite a lot is said about the oxalic acid in spinach and its effect in making the calcium in this vegetable relatively unavailable. Some reference to the fundamental work of the Mellanbys seems essential in a work of this kind, but this and the pioneer work of Miss Harriette Chick on osteoporosis in middle-aged people are omitted. If these defects were corrected the book would be one of the most valuable introductory monographs on nutritional science.

About Cosmic Rays (London: Sigma Books. 1948. Pp. 144. 8*s*. 6*d*.).—In this volume of the Sigma Introduction to Science series Mr. John G. Wilson, PH.D., gives a clear and concise account of the discovery of cosmic rays, and the facts established and theories elaborated about them. The Geiger counter and the cloud chamber, and the ways of using them, are fully described and illustrated. This book can be thoroughly recommended to those interested in atomic physics.

Hernia (3rd ed. London: H. Kimpton. 1948. Pp. 700. 67*s*. 6*d*.).—Surgical books are of three types: there are textbooks giving orthodox teaching, monographs recording the views and experience of an author, and encyclopædias which profess to cover the whole of a subject but should nevertheless make some attempt to separate the chaff from the wheat. This book by Dr. Leigh F. Watson, of Los Angeles, sets out to be an encyclopædia of hernia surgery and it contains as much as the industrious author can get between two covers. "Nature's method of preventing the protrusion of viscera into a preformed sac consists of providing an oblique canal"; "in inguinal hernia the portion of the sac lying within the inguinal canal is called the neck"; "acute coronary thrombosis is sometimes mistaken for a small occult strangulated hernia"; "in infants the obliquity of the inguinal canal is slight, because it passes almost directly through the abdominal wall"; "direct inguinal hernia is infrequent"; "new growths in undescended testes are rare"; "in Great Britain the simple ligature of the sac operation in young infants is usually performed in the Out Patient Department": such statements abound. Dr. Watson seems hazy about the ætiology of indirect inguinal hernia. At one time he says "it is generally believed that all indirect hernias are due to a preformed sac," at another, "in indirect inguinal hernia the sac first bulges at the internal ring . . . on removal of the tension the peritoneum quickly resumes its normal shape . . . on continued repetition of the strain the ring gradually relaxes . . . the peritoneal pouch finally ceases to return into the abdominal cavity." On p. 130 the preformed-sac theory is given, while on p. 131 the balloon theory is illustrated in all its crudity.

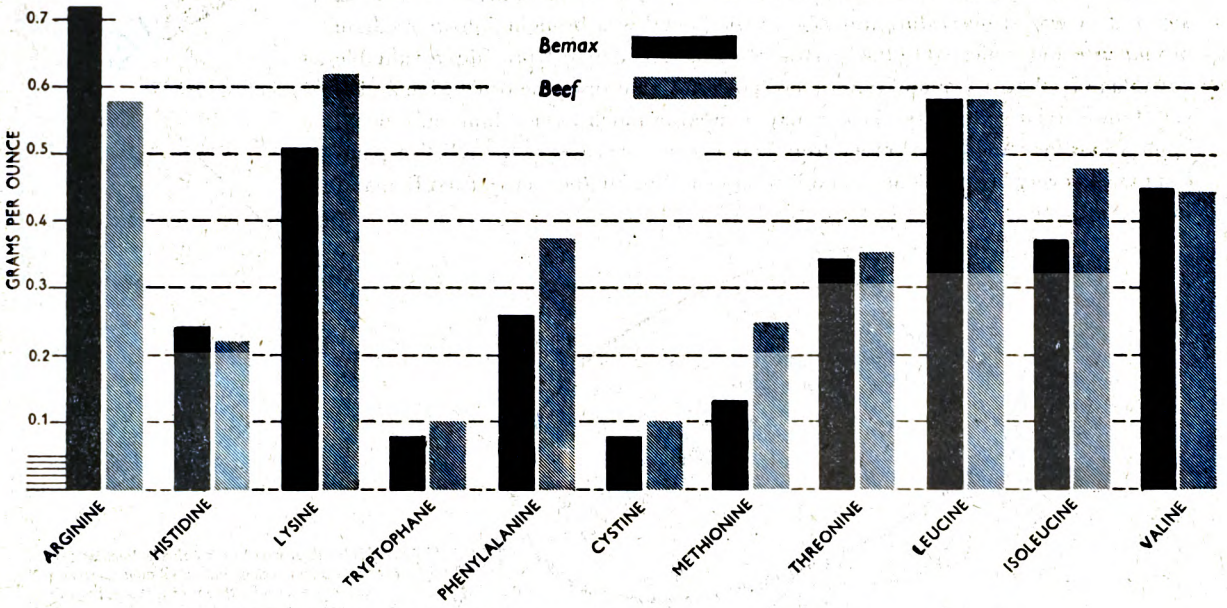
The account of operations is slightly better, but is marred by lack of discrimination, and by a passion both for the new and bizarre, and for the old and quaint. Murphy's button is advocated, and even Moynihan's bone bobbin, that went out of use in 1906. Dr. Watson himself seems to like injecting hernias; he may be right.

1. *Lancet*, 1947, ii, 912 and 1948, i, 678.

Digitized by Google

What is a "first-class" protein?

Compare the essential amino acids of beef and Bemax



Full documentation and/or clinical sample of Bemax may be obtained on application to Medical Dept. 48.B. Vitamins Limited, Upper Mall, London, W.6.

This announcement, the chart and the analyses are copyright.

a single supplement for multiple deficiencies

COMPLEVITE

CLINICAL USES

As a general dietary supplement: in restricted diets, gastro-intestinal diseases: in fluid and light diets: in low fat and other special diets: hyperthyroidism and other states with raised B.M.R.: in chronic infections: throughout convalescence. Also for replacing other preparations of more limited application where full therapeutic doses of the vitamins are not required.

* Amounts contained in the recommended adult daily dose of one tablet of each colour three times a day.

Vitamins Limited

Upper Mall, London, W.6.

Digitized by Google

world-wide local ANAESTHESIA

'Anethaine' was introduced in 1941. The times were grievous, and the need for local anaesthesia was of overriding urgency. 'Anethaine' was brought into immediate prominence and subjected to the severest of tests. 'Anethaine'* provides a valuable advantage in that it is many times more powerful than procaine or cocaine and is yet of lower relative toxicity, since it may be used in much higher dilution. Today, applications for 'Anethaine' range from major operative cases to the relief of pains common to everyday accidents and affections—and in another sense, from England to the Antipodes.

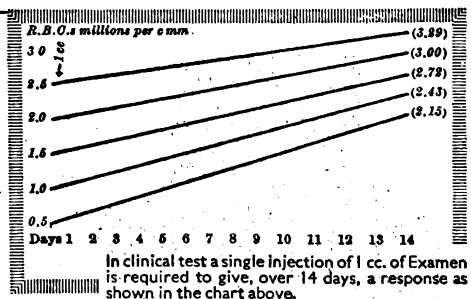
GLAXO

*ANETHAINE brand (Amethocaine hydrochloride). For surface infiltration, and spinal anaesthesia. A new lozenge form for throat and larynx, prior to instrumentation, is now available.

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX, ENGLAND

casting the burden of

PERNICIOUS ANAEMIA



In clinical test a single injection of 1 cc. of Examen is required to give, over 14 days, a response as shown in the chart above.
I = 0.93 – 0.214 Eo where I is the increase in red-blood cells in one week and Eo is the initial red cell count. The formula is derived from Della Vida B.L., and Dyke S.C., *Lancet*, 1942, 2, 275

EXAMEN LIVER EXTRACT is

painless on injection.

proteolysed: preliminary enzyme digestion of the raw liver sets new standards of efficiency in extraction of the active principle.

potent: in the average case of pernicious anaemia in relapse, injections needed only once every 14 days and once every 3 or 4 weeks in maintenance.

protein-free: 'liver sensitization' is exceptionally rare.

standardized: optimum response thus assured.

inexpensive: average cost is four shillings per 1 cc.

fully active in cases with subacute combined degeneration; though, when such neurological complications occur, more frequent injections may be needed.

GLAXO

EXAMEN

1 cc. ampoules: boxes of 3 and 6
5 cc. vials: boxes of 1 and 5

GLAXO LABORATORIES LTD · GREENFORD · MIDDLESEX · BYRon 3434

Digitized by Google

THE LANCET
LONDON: SATURDAY, SEPT. 11, 1948

Private Patients in Health Centres

GRATIFYING progress has been made towards the establishment of an experimental health centre at Stechford, Birmingham (see p. 428). The local health authority has secured a site, and has prepared plans which have been approved by the local executive council. The local medical committee has promised to give the project its full support. The doctors practising in the neighbourhood have discussed the scheme, and enough of them to give the experiment every chance of success would be willing to practise from the centre if terms and conditions of service were satisfactory. The plans have gone forward to the Ministry for sanction and some first inquiries have been made as to the conditions of service in the centre when established. Unfortunately, as we noted last week (p. 399), the answer to one of these inquiries threatens to jeopardise all further progress. The Minister, basing his answer on the strict interpretation of section 21 (1) (*a*) of the Act, which says that it shall be the duty of the local health authority to provide health centres at which facilities shall be available "for the provision of general medical services under Part IV of this Act by medical practitioners," has decided that doctors could not be permitted to treat private patients at health centres. The local doctors feel they could not take service in the centre if this were among the required conditions. Their objection has been sympathetically received by the local executive council, which has unanimously approved a report by its general purposes committee declaring that adherence to this ruling would be detrimental to the health service.

The doctors can bring forward strong arguments on their side. They do not wish it to be believed that they are offering two standards of service—one for N.H.S. patients in the health centre; the other something different, and perhaps better for private patients in their own surgeries. They cannot use their time to their patients' best advantage if they have to duplicate every consulting-hour and be available for one set of times each day at one address and for another elsewhere. Moreover, in these days of domestic difficulties, not least among the vaunted attractions of the health centre was the new feeedom it was said to offer to the doctor's household and particularly to his overworked wife. This is largely lost if consulting-rooms must still be retained, cleaned, and serviced in the doctor's private house while he also attends the centre. If, too, the centre offers, as it should do, a better standard of practice with greater opportunities for mutual help between the doctors practising there, must the patient who has elected to remain a private patient of his own doctor be denied the advantages which the centre offers —always remembering that he, as a rate-payer, is helping to provide them? Lastly, if the doctor is to be required still to maintain private professional premises even though he agrees to work from a health centre, and to pay rent for his accommodation there, he will be facing an extra financial burden which he may find hard to bear. He may regretfully have to refuse the offer of health-centre practice, or the rent for his facilities there may have to be materially reduced below an economic level to allow him to afford the two establishments, in which case the State would in effect, by accepting such token payment for rent in the health centre, be paying a subsidy to help the doctor to provide a separate service at his own surgery for his private patients. This surely is no more defensible than the alternative of allowing the use of the centre for purposes not specifically defined in the Act.

There are theoretical considerations which at first sight might be thought to justify strict adherence to the words of the Act. Undesirable as it is to foster two standards of practice, one inside and the other outside the health centre, even this might be preferable to the risk of encouraging two standards of service, or at least of amenity, inside the health centre. Private patients, it could be argued, if allowed to see their doctors in the centre, would expect prior or better attention than that afforded to patients enrolled under the health service. But need they be given such extra privileges? In the past many doctors have conducted their practices satisfactorily without making distinction in their surgeries or their waiting-rooms between private and panel patients. If in the health centre each doctor is allowed his own suite with its individual waiting-room, he should not find it impossible to continue to give a service satisfactory to both groups of patients, without either group being put at a disadvantage by the other. It might also be objected that problems of administration and remuneration might arise if much private practice was carried out at the centre. The centres will be built and maintained by the local health authority, who will also employ and pay the lay staff. The doctors will use the premises and share the services of the staff. For this they will each pay an agreed charge —probably by a deduction from their remuneration. So long as the doctor's use of the centre is confined to the fulfillment of his duties under part IV of the Act, his share of the expenses is relatively easy to assess, and it could be made to vary directly with the number of patients for whom he has contracted to care. If he is allowed private practice from the centre, it will be very difficult to estimate the demands his practice is likely to make on the centre and its staff; and the calculation of a fair division of expense between the different doctors may well be impossible. But need this trouble the authorities if the doctors can themselves find a way of sharing satisfactorily among themselves, by some partnership or other binding agreement, the over-all charges which are payable for their use of the centre? No greater departure in principle would be needed than has already been made by allowing private practice from State-provided hospitals for the consultant. In fact the same main argument holds good. Mr. BEVAN has defended his action in allowing this privilege to the consultant on the plea that he wished to keep the consultant working inside the service and not having to spend an undue time elsewhere; and that he wished the patient to feel that he could get the best service possible inside premises provided by the National

Digitized by Google

Health Service. Surely the aim should be to give the doctors and their patients, whether health-service or private, the best facilities in general as in specialist practice—and this must mean giving them all access to health centres.

What is needed now is the early establishment and trial of some experimental health centres. The emphasis must be on experiment. No more than a few trial centres are at present feasible. Experiment should be not only in shape, site, or building materials but in ways of running the centre and of ensuring successful coöperation between the patient, the doctor, the lay staff, and the health authority. Can we not as part of our experiment try out the effect of having private patients attending health centres? The risk of their swamping the centre and making undue demands on it is minute. The very small proportion of the community who have elected to remain private patients have mostly done so to avoid having to come to see the doctor: they think it worth paying their fees so that they can still ask him to call for their own convenience. If the experiment showed that private practice in the centre was incompatible with the successful conduct of the centre's other functions, this sanction could be withdrawn before wider health-centre provision was embarked upon. If, on the other hand, the plan was found to work happily, then one of the major obstacles to coöperation by the doctors would have been removed. What is important now is that the Birmingham experiment, which looked so promising and which could still provide a valuable testing ground for our theories, should not be stillborn because of failure to secure agreement over this one point of controversy.

Experimental Megaloblastic Anæmias

THE discovery that folic (pteroylglutamic) acid will cause human megaloblastic anæmia to remit and transform the pathological megaloblastic marrow to a normoblastic state has not, so far, simplified our understanding of the pernicious group of anæmias. On the contrary, a host of new problems has appeared. The evidence makes it clear that neither folic acid nor its naturally occurring conjugate (pteroylheptaglutamic acid) is CASTLE's extrinsic or intrinsic factor —WILKINSON's hæmopoietin. Folic acid relieves the anæmia of sprue, but the failure of fat absorption remains; it will produce a normal blood picture in pernicious anæmia but leaves the neurological part of the syndrome unaffected or worse. Various theories to account for the action of folic acid have been suggested, but they are difficult to test in human disease. It is not therefore surprising that renewed attempts have been made to induce suitable experimental anæmias in animals. These experiments have been helped by the discovery of a folic-acid antagonist in the form of a methylfolic acid.[1] When this antagonist is given to rats the resulting changes in the blood and blood-forming tissues are similar to those produced by a purified diet with succinyl sulphathiazole to prevent bacterial synthesis of folic acid in the intestine. Neutropenia, and not anæmia, is the prominent part of the rat syndrome, so other animals have been tried. The pig has long been regarded as peculiarly suitable for experiments aiming at reproducing human anæmias. WELCH, HEINLE, and co-workers[2] fed three pigs on a purified diet free from CASTLE's extrinsic factor but containing succinyl sulphathiazole and folic-acid antagonist. They claimed that the animals developed a macrocytic anæmia with curious changes in the bone-marrow resembling the megaloblastic change seen in human disease. One of their pigs responded promptly to intramuscular injections of folic acid, one to a mixture of folic acid, liver extract, and nicotinamide, and one to liver extract alone. This was a surprise since chicks, rats, and monkeys with folic-acid deficiency do not respond to liver extracts.

These pig experiments have been repeated under somewhat different conditions by CARTWRIGHT and others.[3] They fed four pigs on a diet low in protein but containing adequate extrinsic factor; they gave folic-acid antagonist and succinyl sulphathiazole as before, and they also took the precaution of preventing their pigs from getting any folic acid for 3–4½ months before the experiments began. The diet did not contain any folic acid, *p*-aminobenzoic acid, or inositol. Eight other pigs received the same diet plus these missing factors and were not given folic-acid antagonist or succinyl sulphathiazole. This group served as a control and they showed no changes apart from some retardation of growth because of the low protein content of the diet. The four pigs did not appreciate their régime. They became weak and listless, their appetite fell off, their coats lost shine, their abdomens sagged, and their squeals became faint and weak. They had diarrhœa, and growth was poor. In 3–6 weeks the animals developed an anæmia which slowly became macrocytic, and the granular leucocytes in the blood diminished. But the most striking changes were in the bone-marrow; here the erythroblasts were increased and the granulocytes proportionately reduced; in addition to the normoblasts there appeared 11–22% of abnormal erythroblasts closely resembling the megaloblasts seen in human pernicious anæmia. These megaloblast-like cells had not been seen in the marrow of animals rendered anæmic by bleeding, nor did they occur in the marrow of the control pigs. When a purified liver extract in relatively large doses was given to these pigs the response varied: one pig showed no change at all, whereas in two others there was a partial remission of the anæmia but the bone-marrow still contained megaloblasts. Folic acid, on the other hand, produced a typical reticulocyte response with remission of the anæmia, and megaloblasts disappeared from the bone-marrow.

The importance of these American experiments is that for the first time an experimental megaloblastic anæmia has been produced—a result attempted but not attained by various methods of resection of stomach and intestine in pigs. This experimental anæmia syndrome resembles human sprue or tropical macrocytic anæmia rather than pernicious anæmia —the signs of nutritional failure, diarrhœa, partial conversion of the marrow to a megaloblastic state, and partial response to large doses of purified liver extract

1. Martin, G. J., Tolman, L., Moss, J. *Arch. Biochem.* 1947, **12**, 318.

2. Welch, A. D., Heinle, R. W., Sharpe, G., Epstein, M. *Proc. Soc. exp. Biol., N.Y.* 1947, **65**, 364. Heinle, R. W., Welch, A. D., George, W. L., Epstein, M., Pritchard, J. A. *Proc. cent. Soc. clin. Res.* 1947, **20**, 7.

3. Cartwright, G. E., Fay, J., Tatting, B. S., Wintrobe, M. M. *J. Lab. clin. Med.* 1948, **33**, 397.

Digitized by Google

are all characteristic of human nutritional anæmia but not of pernicious anæmia. Indeed, CARTWRIGHT and his associates were surprised that their liver extract (which contained no significant amount of folic acid) produced any response at all, because the diet contained adequate extrinsic factor and pig's stomach is one of the richest sources of hæmapoietin.

A similar anæmia has been artificially produced in rats by Dr. WATSON and his colleagues in Prof. L. J. WITTS's department at Oxford. Their technique, which they describe on p. 404, was to fashion an intestinal short-circuit and leave a blind loop; the operative mortality was lowest with a 3-in. loop that filled with peristalsis. The bone-marrow in their animals also contained abnormal erythroblasts resembling megaloblasts. This rat anæmia, too, resembled a nutritional rather than a pernicious anæmia, and in the absence of infection large doses of a purified liver extract produced a remission; a single injection of folic acid was tried in one rat which had responded only partially to liver extract, and its hæmoglobin and red-cell count rose to nearly normal.

Here then are experimental techniques that should at least enable us to find out how folic acid acts in megaloblastic anæmias. There seems little doubt that the odd erythroblasts found in the animals' bone-marrow are of megaloblastic type and are not hyperplastic normoblasts since we know that the latter are not affected by folic acid. The results suggest that there are several ways of producing megaloblastic change in the marrow; it may be—as WELCH [4] has suggested—that folic acid and the anti-pernicious-anæmia liver principle bring about superficially similar results by different paths. The discovery of vitamin B_{12} may mean that there are several substances that can restore megaloblastic marrow to normoblastic. But it is tantalising that when the experimental megaloblastic anæmia—so long striven for by so many workers—has in fact been produced, it is still not of a type that can be used for the standardisation and assessment of liver extracts for the treatment of pernicious anæmia.

International Industrial Medicine

NEXT week more than 700 delegates from 46 nations will attend the Ninth International Congress on Industrial Medicine at the Caxton Hall, London. It is sponsored by the Commission Internationale Permanente pour la Médecine du Travail, which was founded in 1906 as a private society of industrial physicians by LUIGI DEVOTO of Milan; and it is a fitting tribute to BERNARDINO RAMMAZINI, one of the greatest of industrial physicians, that his fellow-countryman should have inspired this international society more than 200 years after his death. The commission now has a permanent committee in each country where industrial medicine is being practised on a large scale. The British committee are the hosts for this congress, the first to be held in Great Britain. The work of the Commission Internationale has often been wrongly associated with that of the International Labour Office, which is officially sponsored by governments, employers, and trade-union organisations in the New and Old Worlds. The I.L.O. probably has made the greater contribution to international industrial medicine by adopting codes of health, safety, and welfare in industry, which it has supported by collecting and disseminating information of international interest. These two bodies exemplify in different ways the efforts made officially and privately to overcome the difficulties of travel and strange tongues and to break down the national frontiers of medicine. Prof. L. CAROZZI, the commission's secretary-general in Geneva, has held together this international fellowship in spite of the long years of war and shortage of funds.

Since the last congress,[1] held in Frankfurt in 1938, there has been a fundamental change in the subjects for discussion, from a limited academic approach to one which not only covers a much wider academic field but is essentially realistic. In 1938 there were 3 sections: occupational diseases, industrial accidents, and a combined section which dealt mainly with predisposition to industrial disease and disability. In the forthcoming congress there are 6: social aspects, occupational environment, medicine and toxicology, nursing, industrial medical practice, and a special section with sessions on the medical content of law and the application of legislation. The congress of 1948 clearly means business. It will discuss the training of industrial medical officers and nurses, and the organisation of industrial medical services. Methods of controlling industrial health hazards are now well established, but they need to be refined and modified so that they may be applied as widely as possible, particularly to the small workplaces which now have little or no continuous health supervision. This is a problem of organisation which might well be raised in the congress discussions. All industrialised countries must face it, for the small workplace is still the backbone of world industry. Industrial accidents as a cause of disability still outweigh occupational disease in importance. High standards of safety engineering alone can never successfully control the human factors responsible for most accidents. Yet the original work by GREENWOOD and WOODS [2] and by FARMER and CHAMBERS [3] on accident-proneness has had very limited applications. Industry and Government must still support fundamental research and not rely too much on established methods.

In the first place medicine served industry by helping to control disease and treating industrial injuries, and these services are still important today, particularly where the risks of accident and industrial disease undermine the health and morale of a particular group, such as coalminers on whose output European recovery largely depends. But the changed concept of industrial medicine's rôle is well illustrated in next week's programme. It includes socio-medical and psychological problems of incentives, work, and skill. Wisely the organisers have included contributions from psychologists and sociologists; for health and efficiency in industry are no longer the prerogatives of doctors, who have welcomed these scientists as colleagues in the battle to raise production. If medicine in industry is to survive and grow there must be radical changes in the training of students and industrial medical officers. So long as

4. Welch, A. D. *Fed. Proc.* 1947, 6, 471.

1. *Dtsch. med. Wschr.* 1938, 64, 1784.
2. Greenwood, M., Woods, H. M. *Ind. Fatigue Res. Bd Rep.* no. 4, 1919.
3. Farmer, E., Chambers, E. G. *Ibid.* no. 38, 1926; *Ibid.* no. 55, 1929.

Digitized by Google

medical students are taught about the rare diseases rather than about sick human beings who have to work, their interests in occupational medicine, both as general practitioners and doctors in industry, will be confined to the treatment of industrial injuries and the investigation of industrial disease. They must be interested in the material and psychological factors which affect the health and efficiency of every working community, not only those inside factory gates and down mines. On their own doorstep the medical profession have the urgent problem of attending to the health and welfare of nurses, the shortage of whom reflects the sad neglect of attention to their working conditions in hospitals. With such an extensive programme there is some danger of these sessions remaining uncoördinated and sealed in water-tight compartments. Improved health and efficiency at work depends on the combined efforts of doctors, engineers, physicists, chemists, psychologists, and industrial nurses. Every effort should be made to integrate these disciplines as far as possible. This can be done to some extent by unofficial discussions, but it is perhaps unfortunate that there is no final session to bring the different experts together in discussion.

In this country, growing social security and the great demands for production have happily reduced the evils of want and starvation, but at the same time that most powerful of incentives—work or want—has lost its force. Industry must find new incentives. "Why men work" is a question which can never be easily answered. Experiment and research, however, have shown that the human relations of working groups, be they industrial, commercial, or educational, have profound effects on the urge to work. Speakers on incentives have entered the congress lists for the first time, and it is to be hoped that this congress will stimulate further research into human relations and will initiate practical experiments in managing human beings in industry. In this sphere more than any other the combined efforts of the medical and social sciences can contribute to the promotion of health and increased production.

Annotations

HOSPITAL-TREATED SICKNESS

STIRLINGSHIRE has been submitted to the punch-card operation. The Glasgow Health and Sickness Bureau which, like its sister in Oxford, works under the auspices of the Nuffield Provincial Hospitals Trust, has prepared a special card in respect of each Stirlingshire patient treated in the year ended Sept. 30, 1947, at a hospital, whether inside or outside the county, and whether inpatient or outpatient. The object was to obtain "a complete picture of all types of hospital-treated sickness occurring among the known population of a given area," and Stirlingshire was chosen as fairly representative of the urban industrial belt of central Scotland. The committee responsible for the study had Prof. Thomas Ferguson as chairman, and nearly all its members were medical men. The report[1] briefly describes the methods used, and sets forth the results, analysed from various angles. The tables show the total volume of sickness treated in hospital (one in every seven of the population received hospital care in the year), the type of sickness and duration of stay in hospital, the geographical factors in hospital treatment, an analysis by age and sex of patients, and so on. There are also supplementary notes on various disease groups, indicating the incidence of diseases per 1000 of the population. The bureau is now engaged on a similar inquiry in the larger and more populous county of Ayrshire. It is suggested that the experience of the Oxford and Glasgow bureaux may be helpful when, as is presumably intended, the regional hospital boards come to build up machinery for keeping and analysing hospital records on standard lines. When this has been achieved "the community should have available reasonably sound guidance about basal hospital facilities that should be provided."

The appearance of this survey offers an opportunity to consider a very wide question. What kind of hospital statistics would really justify the considerable labour involved in their compilation? The Ministry of Health, wisely, has not as yet given any indication of the type of statistical material likely to be required. Miss Nightingale, on her return from the Crimea, was painfully impressed by the lack of scientific coördination in the statistics prepared by the various London hospitals, and for a while she bent her energies towards the introduction of model statistical forms. The general adoption of her forms, she wrote, would "enable us to ascertain the relative mortality in different hospitals, as well as of different diseases and injuries at the same and at different ages, the relative frequency of different diseases and injuries among the classes which enter hospital in different countries and in different districts in the same countries." Her scheme failed—the difficulty and costliness of compilation, and the doubt about the value of the conclusions deduced from such figures as were then published, were no doubt responsible for a gradual loss of interest on the part of the hospitals. Are we much further forward today than in the 1860's? The statistical returns required by King Edward's Hospital Fund for the last fifty years and adopted by many of the hospitals in other parts of the country have afforded much useful financial data, and have been a mine of information on numbers of patients treated, duration of stay, and so forth. But these returns have stopped far short of Miss Nightingale's ideals, and the classification of diseases has lain outside their scope.

It is claimed for the Stirlingshire survey that it should be of service, "as a basic record of hospital facilities actually available and used, in shaping an approach to broad administrative problems of hospital policy, by throwing into relief the general pattern of hospital-treated sickness and suggesting lines of medical and administrative research." It is fair then to ask whether the pilot survey did justify the collection of further data on similar lines. Does the use of a simple card transcribed from the hospital records and fed to the new mechanical sorting devices offer informative results? Do these results go beyond what can be deduced by simpler means, such as those used in the hospital surveys? The latter depended on data of the usual kind regarding the existing hospital facilities, the number of beds available, the occupancy and so on, supplemented by visits to many of the hospitals and a broad assessment of needs based on verbal information as to the pressure on particular categories of accommodation. The waiting-list is a notoriously unreliable guide, but indications of pressure in one direction or another, such as can be obtained direct from the hospitals, is a very relevant factor. The Stirlingshire survey is based on the assumption that the new mechanical methods can offer data not hitherto available to those who have to plan the hospital services of the future. Without a detailed knowledge of local conditions it would be presumptuous

1. Hospital and Community. 1. Hospital-treated Sickness Amongst the People of Stirlingshire. 1948. Pp. 96. 3s. 6d. Nuffield Provincial Hospitals Trust, 13, Mecklenburgh Square, London, W.C.1.

Digitized by Google

to offer a verdict, but the sceptically minded will run through the "results" without much conviction.

The practical usefulness of any system of statistical records cannot be too frequently or too insistently questioned. We live in an age when the urge towards the collection of statistical data can easily run riot, and there is danger that time and trouble may be thought fully justified if it produces data not previously available, irrespective of their practical usefulness. It would be a great help therefore if we could have from the committee responsible for this latest and admittedly pilot survey a direct and positive statement of the conclusions they draw. Do they, in the light of their local knowledge, feel that the results they have set down are of sufficient practical importance to warrant further experiment along these lines? Is this analysis of an existing hospital service really a help in deciding what ought to be, or will be, provided tomorrow? The publication of the survey unaccompanied by the committee's own verdict may lead others to follow suit without a clear perception of the ends likely to be attained.

POISONOUS BERRIES

ALMOST every summer brings its crop of accidents, sometimes fatal, through the consumption of poisonous berries, often mistaken for blackberries. This summer is no exception. The account, on page 438, of two incidents of this sort in the south of England is, however, notable for the survival of the children who consumed the berries of the Deadly Nightshade, while the child who ate those of the usually less poisonous Woody Nightshade died.

All the nightshades belong to the family solanaceæ and are more or less poisonous, except Enchanter's Nightshade (*Circæa lutetiana*), which belongs to a different order and is not poisonous. Two genera of the solanaceæ are found as weeds in England—atropa and solanum. *Atropa belladonna* is considerably rarer than the several species of solanum and thus provides fewer cases of poisoning; this is fortunate because all its parts, especially the berries, are poisonous and it lives up to its popular name of Deadly Nightshade. The solanum weeds include *S. dulcamara*, the commonest, and *S. nigrum*, whose folk-names are somewhat muddled; *S. nigrum* is called Common Nightshade, Black Nightshade, Woody Nightshade, and Bittersweet, the last two names being shared with *S. dulcamara*. Cultivated species include *S. tuberosum* (potato), and *S. lycopersicum* (tomato). The poison has been found in unripe potatoes and in the young shoots, leaves, and stems of the plants. Another cultivated solanum, the Wonderberry, something like a large bilberry, was discarded soon after its introduction some thirty or forty years ago, through fear of possible poisoning. For the same reason tomatoes were long cultivated as ornaments, under the name of Love Apples, before they were eventually accepted as food.

The active poison of Deadly Nightshade is atropine, and that of Woody Nightshade and Black Nightshade solanine. Deadly Nightshade may be distinguished by its corolla, which is bell-shaped, whereas those of the solanum nightshades resemble the potato plant's. The berries of Deadly Nightshade are black, shiny, and about as large as a cherry. Bittersweet (*S. dulcamara*) has a woody stem, alternate cordate leaves, and red oval berries ½ in. long, and it straggles over other plants in hedges and thickets. Its drooping clusters of flowers are borne on a stem which usually arises opposite a leaf. The petals are either white or lilac-blue with a green spot on the base of each surrounding a yellow cone of anthers; the poison is chiefly concentrated in the berries. The dried stems are official in the *British Pharmaceutical Codex*. There is a maritime variety with a prostrate stem.

Black Nightshade (*S. nigrum*) has white flowers and black globular berries, which are also poisonous, about the size of haws. Its stem is not woody and its leaves are ovate. Varieties with red and with yellow berries are known, such as the Jersey variety with dentate leaves and scarlet berries.

When it is suspected that a child has swallowed the berries of one of the solanum family, what should be done? For practical purposes all solanum berries are poisonous. The immediate necessity is to empty the stomach as effectively as possible; remembering that whole berries or large fragments of them will usually not pass through a stomach-tube. Thereafter the child should be kept under close medical supervision, preferably in hospital.

AN EAGLE IN THE DOVECOTES

"THERE is no force so great as that of an idea whose hour has struck," Mrs. Margaret Sanger quoted, at the congress on Population and World Resources reported in these columns last week. She might have added that the force of an idea derives from human personalities—sometimes, it almost seems, from one personality. She was recalling the history of family planning in America, of which she has been the pioneer. In Great Britain we have been fortunate in that family limitation has never been regarded as a crime. Things were different in America thirty years ago, when Margaret Sanger is reported to have "appeared on the horizon with three children in her arms and a wild look in her eye." She had been working among the poor in New York, and had been dismayed at the unnecessary burden and suffering borne by women, and dreaded by them for their daughters, in slums where pregnancy followed pregnancy and poverty deepened with each child. She was ready to challenge the Comstock laws which for thirty-five years had blighted free discussion of human relations and sexual ethics. Anthony Comstock, she said, had ideas about purity and was determined to enforce them. Abortion, even on therapeutic grounds, the practice of contraception, and the sale of contraceptives or of publications about contraception were punishable by long imprisonment and heavy fines. Since it was illegal to send any printed matter about contraception through the post, a large government staff was kept busy opening other people's letters and parcels. An editor of 70 was sent to the penitentiary for starting a journal—"Dr. Blacker please note"—called the *Eugenics Review*. The same fate befell the editor of a free-thought weekly, because he challenged Comstock. Margaret Sanger was indicted for publishing a little monthly insisting on the right of women to space their families. She was determined to tell them how to do it, too, but a hunt through the libraries for information produced only a small book pointing out how wonderful it was to have children.

Conditions in a city which prided itself on its municipally owned apartment houses were a cynical comment on this find: the apartments were built to take parents with no more than four children; if they exceeded the ration they were asked to move, and by the time they had seven or eight they were living down in the shipyard slums. Margaret Sanger's trial was postponed, and she seized the moment to write a pamphlet on family limitation, which was printed and packed up for mailing before she sailed for Europe to prepare her defence. When she was well in the middle of the Atlantic the pamphlets were posted, the recipients including the judge, the district attorney, the President, and Mr. Anthony Comstock. In England she was welcomed by a group of warm admirers, Havelock Ellis, H. G. Wells, Edward Carpenter, Gilbert Murray, the Drysdales, and Dean Inge among them. By the time she returned for her trial feeling in the United States was so strongly in her favour that the case was dropped. "I am sure Mrs. Sanger won't do this again," said the district attorney. "I assure you I shall," she replied, and soon afterwards opened, in New York, the first practical birth-control

Digitized by Google

clinic in the U.S.A. It was closed by the police in ten days, and Margaret Sanger and her associates went to prison, where they hunger-struck and appealed, and won a small momentous decision: that if she had been a doctor it would have been all right to give advice on contraception to married people for the cure and prevention of disease. This was the first crack in Comstockery, and it widened fast to let in daylight. The clinic was opened again under the charge of Dr. Hannah Stone, who remained there till her recent death. There are now some 600 clinics in the United States, several hospitals are legally able to give contraceptive courses if they wish, and the whole attitude to the subject has become more rational.

Those who listened to this indomitable and charming speaker recounting her campaigns found it easy to recognise the qualities that have brought her victoriously through them.

A NEW DISEASE?

FROM Australia comes the report of a new mycobacterial infection in man.[1] During the last few years 6 patients have been seen in rural districts of Victoria with an indolent ulcer of the extremities suggesting tuberculous infection. Microscopic examination showed very numerous acid-fast bacilli, which could not at first be recovered on culture and which were not pathogenic to the guinea-pig. Indeed their appearance was reminiscent of *Mycobacterium leprae*, but the clinical picture was unlike that of leprosy. This diagnosis was definitely excluded, first by injecting into the rat infected material, which gave rise to ascites and superficial lesions of the legs and scrotum, and secondly by successful cultivation of the organism, at 33°C, on several media suitable for *Mycobacterium tuberculosis*. The epidemiological picture is far from clear. Although 4 of the patients came from a single rural neighbourhood and the other 2 from a second, no common factor of contact or association could be found; and no disease which could be connected with their's was detected among animals in these areas. Search for previous accounts of any similar disorder brought to light only a remark that in one part of Queensland several patients had been seen with a single small ulcer containing "organisms indistinguishable from *Myc. leprae*." The present report certainly seems to justify the authors' claim that this disease has not hitherto been recorded. Apart from poisoning by one of the new agents in industry, a new disease is most likely to be due to an organism which either has newly learnt the art of preying on man, or else is so rare or has so remote a habitat that it has previously escaped detection.

GLYCOSURIA IN PREGNANCY

THAT glycosuria is found more often in the pregnant than in the non-pregnant woman has long been known; but the mechanism and the frequency of this phenomenon are still uncertain. Using Fehling's test, Weiden [2] found sugar in 6·9% of 172 specimens from non-pregnant women, compared with 29·6% of 340 specimens from women in the first trimester of pregnancy, 19·8% of 51 specimens in the second trimester, and 21·4% of 145 specimens in the third trimester. Of a small series of 39 women in whom the urine was tested throughout pregnancy, 9 had glycosuria which disappeared towards full term. The effect of the ingestion of 50 g. of glucose upon the incidence of glycosuria was investigated in 102 patients, of whom 11% had glycosuria in the fasting specimen during early pregnancy, and 15% had glycosuria in the later months. After ingestion of glucose, glycosuria was found in over 60% of the entire group. The fasting blood-sugar of 103 pregnant women ranged from 40 to 120 mg. per 100 ml.; but in 38% of these the level was 80 mg. per 100 ml. or lower. Of 24 women who were re-examined after the end of pregnancy, 19 had a fasting blood-sugar of 90 mg. per 100 ml. or more.

Glucose-tolerance tests were done on 102 women. In almost half of the 38 without glycosuria, the maximum figure during pregnancy did not exceed 140 mg. per 100 ml., and in almost every case the curve had returned to normal a year after the end of pregnancy. The renal threshold was lowered in 33; and 19 had curves classified as "renal glycosuria with superimposed diabetes"—i.e., the blood-sugar did not return to normal within two hours, yet the maximum figure never exceeded 180 mg. per 100 ml. Post-partum curves in these patients were of the same type. In 7, curves resembling the Maclean lag-curve, with peak figures exceeding 180 mg. per 100 ml., were obtained.

The striking feature of these observations is the frequency of lowered glucose tolerance, even in women without glycosuria. Laferty [3] has suggested four factors that may be responsible for the phenomenon: (1) heavy withdrawal of glucose from the maternal blood to nourish the fœtus; (2) excessive consumption of glucose by the mother; (3) excessive withdrawal of glucose from the maternal blood through over-production of insulin; and (4) insufficient supply of glucose due to faulty alimentation. Of the many other theories which have been advanced, two are controverted by the Melbourne findings: one is that this disturbance is due to excessive mobilisation of glucose, and the other that a raised blood-sugar plays an important rôle. These findings imply that restriction of carbohydrate intake during pregnancy is fraught with the danger of acidosis. They do not invalidate the sound rule that a glucose-tolerance test should be performed on every pregnant woman with glycosuria.

BIRTHDAY GREETING

To mark his 80th birthday, Sir John Parsons was presented with his portrait at a reception held in his honour at the Royal College of Surgeons, Lincoln's Inn Fields, on Sept. 3. The portrait, which was painted by Mr. John Gilroy, was the gift of the Faculty of Ophthalmology and of the Ophthalmological Society of the United Kingdom.

It is given to few men to excel in all the branches of their specialty as Sir John Parsons has done. His advice has been sought by patients all over the world, and his views on scientific problems are accepted by physicists and physiologists alike. His work on colour vision is still perhaps the best unbiased account of the conflicting theories of other workers, and for his studies on the theory of perception and of illumination he was elected president of the Society of Illuminating Engineers and admitted to the fellowship of the Royal Society—a rare distinction for a practising clinician. He represented British ophthalmology to other nations, and the Medical Research Council regarded him as one of their most valuable members. Indeed he interested the council in ophthalmic research and has seen to it that that interest was maintained up to the present time. Now his dreams are coming true—two of them quite recently in the shape of an Ophthalmic Institute and the establishment of the F.R.C.S. in ophthalmology. His colleagues, who are still his students, are glad to have his encouraging smile to cheer them on, and all the profession join in their wish of "Many more happy birthdays."

1. MacCallum, P., Tolhurst, J. C., Buckle, G., Sissons, H. A. *J. Path. Bact.* 1948, **60**, 93.
2. Weiden, S. *Med. J. Aust.* 1948, **1**, 646.
3. Laferty, J. M. *Amer. J. Obstet. Gynec.* 1931, **22**, 637.

THE INDEX and title-page to Vol. I, 1948, which was completed with THE LANCET of June 26, is now in preparation. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Digitized by Google

Special Articles

COMPENSATION FOR INJURY *

H. C. WARDLEWORTH NUTTALL
F.R.C.S., D.P.H.
CONSULTING SURGEON, ROYAL LIVERPOOL UNITED HOSPITAL

THE present system of dealing with claims for compensation for injury is unsatisfactory, and the National Insurance (Industrial Injuries) Act, 1946, will perpetuate some of its weakest features.

Under the present system an injured workman, after reporting the accident to a representative of his employer, consults his panel doctor, who furnishes him with a certificate on which weekly compensation is paid. If there is any dispute the workman consults a solicitor, who formulates a claim. In the event of the employer's resisting the claim the case goes to arbitration, with the production of opposing medical evidence and occasionally the assistance of a medical referee. Common-law cases follow a more or less similar course, save that they are tried in the High Court, and it is a question of damages rather than compensation.

Workmen's claims under the new Act will be dealt with by an industrial pensions officer. They must be accompanied by a medical certificate, and the applicant may have to submit to examination by an appointed medical officer. The decision of the pensions officer will be subject to appeal to a local appeal tribunal of employers and workmen, with two coöpted medical practitioners when necessary. The medical assessment for pension will be made by a medical board, probably the medical board of the Ministry of Pensions. There will be a right of appeal against a final assessment to a tribunal consisting of a chairman of a local appeal tribunal and two medical practitioners. There is no lump-sum compensation under the new plan.

THE CLAIMANT

The great majority of British working men and women, being normal healthy people, remain on the compensation list as short a time as possible. They would feel ashamed to take a penny under false pretences, and are only too anxious to continue working if possible. There are, however, many circumstances which may influence even normal people to persist in a claim after they have recovered, and there is always a proportion of abnormal people among the injured. For instance, the Workmen's Compensation Act makes no allowance for a man's running into debt, and this is inevitable if the incapacity lasts at all long. He is then faced with arrears of payment to tradesmen which it would take years to pay off out of his normal wages; and, unless a lump sum is forthcoming, he feels that his only chance is to persist with some complaint or other till he gets redress. During and since the war many people, particularly married women, have been forced into occupations which they dislike and naturally welcome a chance of evading. Many other cases are probably psychopathic misfits, self-centred, lazy, and mutinous, who lag behind or lack the skill to compete on even terms with their fellows.

THE DOCTOR AND DIAGNOSIS

The first doctor consulted by the claimant is of fundamental importance, and often it rests with him whether there is a claim or not; and, if there is, whether it is valid or not. Even today many doctors in the poorest districts are not sufficiently independent and are consciously or unconsciously influenced in giving certificates.

The diagnosis in many cases of injury may be simple, but prognosis is always difficult and may be impossible without specialist training. It is, however, on the prognosis that the case may be fought. Moreover, even the simplest case may be complicated by exaggeration or malingering. The doctor can scarcely be blamed for playing safe in cases of doubt. His remedy is to get a second opinion when the doubt warrants it.

It is most important to obtain a correct history of any accident. In most instances the type and degree of violence are directly related to the effects and could be predicted, or conversely the violence could be assessed from the effects produced. For example, many types of fracture, such as the fracture-dislocations of the ankle, are now known to be related to particular strains or types of violence. The converse is not so well established, and it is always of great value to elicit as far as possible the direction and degree of any force acting in any particular case, and to observe whether the description tallies with the alleged effects or not.

Case 1.—A man reported that he had fallen aboard ship and injured his right shoulder two months earlier; he had been radiographed at a cottage hospital and told that there was a fracture of the upper end of the humerus. He had been transferred to another local hospital, where radiography had been alleged to show fracture of the glenoid also. The patient had provided himself with copies of the radiological reports.

Careful and critical elucidation of the history of the accident revealed that he had fallen flat on his back. Examination showed extraordinary development of the muscles of both shoulders, more particularly those muscles concerned in movements of the shoulder blades, and that this abnormal development was equal; there was no wasting on the injured side; movements of the injured shoulder were free but not carried out at the true shoulder-joint but by means of an extraordinary or abnormal movement of the shoulder blade, so that in full abduction of the arm the lower angle of the bone projected two or three inches beneath the skin. In other words there was complete fixation of the true shoulder-joint. This conceivably could have followed a fracture of the upper end of the humerus with or without the glenoid, but the unusual development of the muscles and the wide range of movement had obviously been gradually developing for a much longer time than two months. Routine examination of the other shoulder disclosed complete fixation of the shoulder-joint with a full range of movement by means of abnormal shoulder-blade movements.

This strongly suggested that there was some identical cause for the similar condition in both shoulders and threw strong doubt on the probability of any accident. Radiography of both shoulder regions showed that the upper ends of both humeri and the glenoid cavities of each scapula were greatly deformed. The upper ends of the humeri were reduced to mere points, and the heads of the bones had run down the shafts like melted wax. A similar appearance was seen in the glenoids, and it was diagnosed as a type of melorheostosis of Leri. There was no sign of fracture or injury.

Errors in diagnosis were made in this case by not eliciting a correct history, and by neglecting to follow the routine principle of comparing one limb with the other.

A much more serious result of wrong diagnosis in the initial stages is delay caused by neglect or by incorrect treatment, as in the following case:

Case 2.—A workman fell and sustained a fracture-dislocation of his shoulder.[1] The dislocation was missed on radiography at the cottage hospital. The arm was bandaged, and later the patient was referred to an orthopædic surgeon, who discovered the dislocation by radiography but too late to reduce it. At the arbitration compensation was refused on the grounds that the negligence committed in the cottage hospital constituted a novus actus interveniens; hence the present incapacity was due substantially to bad medical treatment and not to the original injury.

THE SOLICITOR

Whereas the doctor takes a rather detached view of any question of compensation, the lawyer jealously watches his client's economic interests. In many instances solicitors have been grossly misled by medical certificates

* Abridged from a paper read to the Wrexham and District Clinical Society.

1. Rothwell *v.* Caverswall Stone Co. Ltd., 1944, 2 All E.R. 308.

Digitized by Google

based on inaccurate diagnoses from various causes but chiefly from lack of special experience in these cases. They can scarcely be blamed therefore if they take up weak or even mistaken cases at times. There is unfortunately another side to it, and when it is remembered that it costs at least £20–30 to defend a county-court action, it is not surprising that in about 98% of cases the employer submits to the workman's claim being settled without a judicial decision. As Collie asks, "Is it unreasonable to suggest that a large proportion of the cases in the 98% are settled by processes which might be described by an ugly word?" Colour is lent to this view by the obvious preparation some workmen have undergone before they come for a medical examination. In fact their solicitors have such a poor opinion of their case that they have been told not to answer any questions at all for fear they should give themselves away.

WHEN DOCTORS DISAGREE

It has become a byword that doctors agree to differ, and it must often appear to the legal mind, untrained in medicine, that opposing medical experts were disagreeing about simple facts without any apparent justification. As Kitchin says, "One of the saddest sights in the administration of justice is two processions of medical witnesses, one on each side, in a personal-injury case or a murder trial where the prisoner has pleaded insanity, flatly contradicting one another on fundamental matters of fact." [2]

In these cases, however, there is plenty of room for wide differences of opinion, even when the opposing witnesses are evenly matched in training and experience. When, as so often happens, one of the witnesses, either so-called expert or general practitioner, is expressing opinions on subjects of which he cannot, from lack of training or opportunity, have any adequate knowledge, it is not surprising that agreement cannot be reached.

Case 3.—A man, aged 31, stated that in February, as he was passing a stationary lorry on his pedal cycle, the driver of the lorry opened the offside door and knocked him off his bicycle, and he sustained a sprain of his left wrist, bruising of his left hip and knee, and a sprain of his left ankle. He was able, however, to pick himself up and, after talking to the driver, rode his cycle home. He consulted his panel doctor, who treated him, but he was not referred to any hospital. In March, exactly a month after the accident, he was referred to me complaining that he had no grip in his left hand, his left hip was sore, and his left knee very painful. The ankle was better, though it had been swollen.

His general condition was fair, though he was poorly nourished; and there was no sign of any traumatic neurasthenia. He had a bandage round his left wrist, but the joint was normal in all respects, and there was no limitation of movement of wrist or hand. All bruising about the left hip had disappeared, and movements in all directions were free and painless. There was a bandage round his left knee, but the joint was cool to touch, there was no swelling or effusion, all movements were free and painless, and there was no wasting of the thigh muscles. The left ankle was normal, and he bore weight well on the limb, though at first he pretended he could not do so.

I reported that he was malingering; from the history of the accident he could not have hurt himself much; otherwise he could not have ridden home. Moreover his demeanour was unsatisfactory, and he was very guarded in his answers to questions and appeared to be lying most of the time. Even when I asked him if his bicycle had been damaged, he had to think for quite a time before he said it was not.

In September his solicitors wrote to say the case was down for hearing at the forthcoming assizes. They enclosed a report from the medical officer of a county hospital to the effect that the patient had been admitted in mid-August with a history of frequency of micturition, hæmaturia, and pain in the lower abdomen dating from May (three months earlier). Radiography suggested renal tuberculosis, and this was confirmed by finding the bacillus in the urine. In the opinion of the medical officer there was no evidence of any disease or disability following the accident and no connexion between it and the tuberculosis of the kidneys.

At the trial in October two general practitioners and the medical officer of a sanatorium, to which the patient had in the meantime been admitted, gave evidence to the effect that the shock of the accident had caused an anxiety neurosis, which had lowered his resistance to tuberculosis, which had been latent before the accident. Against this purely conjectural assumption the following facts were submitted: (1) From the history of the accident there was no evidence of any serious injury or shock; (2) when the patient was carefully examined exactly four weeks later, there was no sign of any injury, no abnormal mental state, and no complaint of any urinary symptoms; (3) in tuberculosis of the kidney urinary symptoms appear early, whereas in this case they did not arise till May, 3½ months after the alleged injury; and (4) renal tuberculosis is a blood-borne infection, and the evidence is against trauma being an ætiological factor—in any event there was no evidence of any injury to either kidney in this particular case.

The judge thought the disease was bound to come on sooner or later, but he was satisfied that the accident was a direct cause of the anxiety neurosis, which in turn accelerated the onset of the disease, which would probably cause death earlier—perhaps much earlier—than otherwise would be the case. The plaintiff was awarded £1568 damages.

A case of this kind is a fairly straightforward surgical problem, and any fully trained surgeon would find little difficulty in coming to a contrary opinion on the facts. For a layman without that scientific training it would be impossible to assess the surgical issues or the expertise of the various witnesses. I therefore do not complain that the workman was given the benefit of the doubt. I am mortified that the "doubt" should hang on such an old cobweb as "anxiety neurosis."

Case 4.—A workman, aged 45, was holding the shafts of a handcart while it was being loaded. By mischance a very heavy weight was suddenly dropped on the other end; the shafts went up, carrying the workman with them, and then dropped again as the weight rolled out; he landed heavily on his feet. Though he complained of some pain he continued working for several days, limping on his right leg. He then ceased work, was examined by various doctors, and was treated at different hospitals until, about eighteen months later, he was referred to me. He then complained of weakness and twitching of his right leg. Even while he was sitting quietly in a chair his right leg was constantly shaking and his right heel tapping on the floor.

Examination revealed no sign of any organic lesion; and when his attention was distracted the clonic spasm of the leg ceased. I reported a functional condition; this was denied, and before the arbitration a well-known orthopædic surgeon was asked to examine him. He did so and agreed to attend the hearing. The evidence on the other side was to the effect that the workman had an organic nerve lesion as the result of the accident. This was supported by a Ministry of Pensions neurologist, who averred in evidence that all reflexes were absent in the affected limb. We denied this, and the judge decided that, since the medical evidence was so much at variance, he would see the man in his private room to allow the medical witnesses to demonstrate their findings.

The patient was laid on a wooden table, his right heel beating a tattoo all the time. The Ministry of Pensions neurologist showed that it was impossible to demonstrate any of the reflexes owing to the great spasticity and clonic spasm in the limb. The orthopædic surgeon was faring no better, when I remembered that if the patient's attention was distracted the clonus would probably stop. I therefore walked over to him, tapped him on the shoulder, and said "I thought you told me the handcart was painted red when as a matter of fact it was green." He was so indignant at this gross misstatement that he at once became involved in a spirited argument, during which the limb gradually ceased twitching and the orthopædic surgeon was able to demonstrate the Babinski, patellar, and gluteal reflexes and to show that there was full movement at all joints and no spasticity whatever. While the neurologist was being revived the judge remarked that "Whatever the man was suffering from, he was satisfied it was not an organic nerve lesion."

Case 5.—A dock labourer, aged 72, was said to have had his left hand trapped between a stanchion and a skid and to have

2. Kitchin, D. H. *Med. Annu.* 1942, p. 208.

Digitized by Google

sustained a fracture of the terminal phalanx of his ring finger and bruising of his thumb leading to osteo-arthritis.

At the county-court arbitration three years later it was claimed there was now a subluxation of the carpometacarpal joint of the thumb. An expert witness for the workman gave evidence to this effect and produced radiograms of both hands to support it. In addition he stated that the radiologist had positioned the hand specially to show the subluxation, and had reported its presence, and a radiogram of the other thumb had been taken for comparison.

When I had previously examined the thumb I had not found any subluxation, and I examined it again in court with the same negative result. Inspection of the films produced made it clear that the film of the left thumb did not show any subluxation. Moreover it was impossible to make any exact comparison with that of the right thumb, since it was not in a similar position, as could be seen by the way the shadow of the right thumb was superimposed on that of the index, whereas that on the left side was not. I pointed out that the radiologist was well known to me, and I was sure he would not have given any opinion about a subluxation on those films, and I refused to accept the statement without seeing the report. The report was not produced. Nevertheless the workman was awarded a small weekly payment for partial incapacity.

The radiologist's report turned up later. It merely stated that there was slight osteo-arthritic changes in the metacarpo-phalangeal joints of *both* thumbs. There was no mention of the carpometacarpal joint or of any subluxation.

These examples emphasise the necessity for a long and wide experience of all varieties of injury, particularly those in which there is no question of compensation. For many years I kept records exemplifying all types of mutilation and deformity. It was a never-ending source of interest to see the wonderful adaptability displayed. One of the most amazing was a plumber whose hands were apparently totally crippled by gout. Both hands were almost completely clenched owing to contractures of all the fingers and both thumbs; he could just separate the tips of his fingers from the palm for about $^1/_2$ in.; and yet I saw him "wipe" a joint on a leaden water pipe as well as any plumber could.

Many such patients would obtain substantial compensation or heavy damages if there were any question of injury. Sadder to relate, it is unlikely that they would be any longer usefully employed.

ASSESSMENT OF DISABILITY

Tables have been drawn up giving the percentage disability for various amputations of the limbs, from a finger to the whole limb. In practice these methods are useless. For instance, loss of a finger would be very serious to a violinist or a pianist, but comparatively trivial to a porter or a dock labourer. Each case should be dealt with on its merits and with regard to the type of work involved or possible. Here again a fairly wide acquaintance with different pursuits, crafts, and labour is extremely valuable.

There is also an unfortunate tendency to classify any particular injury in terms of its most serious or complicated manifestation and to ignore the simpler types. Fractures of the os calcis are notorious in this respect: those that are comminuted and involve the subastragaloid joint with subsequent arthritis live up to their evil reputation and cause serious permanent disablement; whereas simple breaks through the posterior part of the bone which do not involve joints cause little if any disability.

Case 6.—An R.A.F. pilot on a visit to a lady friend found it convenient to leave by the window to avoid embarrassing the lady's husband. This involved a drop of about 20 feet and caused fracture of the os calcis on both sides. Nevertheless he was fit for duty three weeks later.

Fractures of the spine also vary enormously in the real disability they cause. Most cases, even of crush fractures of the vertebræ, may cause little incapacity once they are consolidated, whereas the comparatively trivial fractures of the lumbar transverse processes often draw compensation for two or three years.

MEDICAL REFEREES

It might be thought that the appointment of medical referees would have avoided many of the difficulties I have described. Unfortunately this is not so, and the explanation is simple. First, no one man is sufficiently experienced or qualified to act in all cases; this could be got over by appointing specialists in each branch as required. Secondly, the remuneration is wholly inadequate, compared with the likely earnings of an experienced man (and it is obviously no use appointing anyone who is inexperienced). For these reasons we find a general practitioner or a physician acting as umpire in surgical cases in which their teachers often appear as experts. No wonder many eminent physicians or surgeons refuse to touch compensation work, whereby they might be made to appear ridiculous.

MALINGERING

When the claimant is malingering, a particular movement of a joint, ability to bear weight, &c., may be observed only once in the consulting-room, after which the claimant is on his guard, and in court it may not be possible to demonstrate it again. Alternatively, if it is successfully demonstrated, the judge, counsel, &c., often miss the point from lack of medical knowledge.

A malingerer seldom gives himself away so completely as in the classical case in which the counsel for the employer, during a gruelling cross-examination, suddenly asked: "You say you have been unable to raise your arm at all since the accident—well, how high could you get it before?" Without thinking, the man instantly put his arm freely above his head.

APPRECIATION OF MEDICAL EVIDENCE

Anyone with a sense of history must look with some envy on the medieval mummery lingering in the courts and think how wonderful it would have been to see a surgeon performing a gastrectomy in a full-bottomed wig. But why after having administered the oath with all the solemnity of bell, book, and candle, do they

> "Assume that the witnesses summoned in force
> In Exchequer, Queen's Bench, Common Pleas, or Divorce,
> Have perjured themselves as a matter of course"?

The plain fact is that medical evidence is appreciated only with great difficulty, if at all, by lay tribunals. In these cases the doctor is in a false position; after years of training in scientific methods his clinical observations and opinions are judged by men whose whole outlook has been classical and academic and who, like the schoolmen of the Middle Ages, are more conversant with books than with nature. For instance, I have heard eminent counsel argue that, since the practitioner had examined a patient many times, he must know more about his injury than the expert who had examined him only once. And even a county-court judge once claimed that two general practitioners and a house-surgeon were a good working majority against an experienced surgeon in a complicated surgical case.

CONCLUSIONS

Cases of injury involving compensation are essentially difficult and should receive specialist attention from the beginning and during rehabilitation.

It is unfair to expect general practitioners to treat or assess disability in these cases.

The suggestion in the new Act to remove these cases from the courts is strongly supported by medical experience in the past and, so far as assessing disability is concerned, should include common-law cases also.

Digitized by Google

The medical tribunals should be carefully chosen from among specialists with wide experience in treating and examining these cases; though they must not, of course, assess the disability of their own patients.

If the new Act will remove workmen's compensation cases from the courts it is to be welcomed. But unless the personnel of the medical boards is very carefully selected there may be great hardship for many working men, or alternatively a third of the population may become pensioners of the remainder.

DISTRIBUTION OF STREPTOMYCIN

THE Ministry of Health announces that in future streptomycin will be allocated and distributed by regions. In each region beds in stated hospitals "will be so staffed and equipped as to ensure the necessary scientific control of the treatment. It is therefore hoped that, so far as possible, doctors having suitable patients will endeavour to admit them to these beds." The number of beds and cots allocated and the distribution centres are as follows:

Region	*No. of beds*	*Distribution centres*
Newcastle ..	68*	General Hospital: Mr. Wing, chief dispenser (Newcastle 35211). Royal Victoria Infirmary: dispenser (Newcastle 25131). Pathological Laboratory, Cumberland Infirmary, Carlisle (Carlisle 590).
Leeds ..	68	Blood Transfusion Laboratory, Bridle Path, York Road, Seacroft: Dr. T. S. Marshall (Leeds 45091).
Sheffield ..	74	City Hospital, Hucknall Road, Nottingham: Dr. W. Morton (Nottingham 66292).
East Anglian	38	Addenbrooke's Hospital, Cambridge: Mr. Hopkins, chief pharmacist (Cambridge 4451).
North-West Metropolitan	138	West Middlesex Hospital, Twickenham Road, Isleworth: Miss Bristowe (Hounslow 2311).
North-East Metropolitan	64	Mile End Hospital, Bancroft Road, E.1: Dr. W. G. Sears, physician-superintendent (Advance 2873).
South-East Metropolitan	67	Grove Park Hospital, S.E.12: Dr. M. H. Logg (Lee Green 1547).
South-West Metropolitan	66	South London Blood Supply Depot, Benhill Avenue, Sutton: Dr. E. G. Murphy (Vigilant 0068).
Oxford ..	80	Churchill Hospital: Mr. Trillwood, chief pharmacist (Oxford 48651).
South Western ..	56	Ham Green Hospital and Sanatorium, Bristol: Dr. J. Macrae (Bristol 31165).
Wales ..	57	Cardiff City Isolation Hospital: Dr. Emrys Harries (Cardiff 960).
Birmingham ..	90	Selly Oak Hospital: Mr. R. P. S. Kelman, medical superintendent (Selly Oak 1361).
Manchester ..	60	Royal Infirmary: Mr. J. B. Lloyd, chief pharmacist (Ardwick 3300).
Liverpool ..	50	Fazakerley Sanatorium: Dr. O. F. Thomas, medical superintendent (Aintree 2324).

* Incomplete return.

The Ministry suggests that the greatest potential danger is the production of streptomycin-resistant strains of *Mycobacterium tuberculosis*. "Thus a patient with very early pulmonary disease who might have responded to other recognised forms of treatment alone but who is given streptomycin 'prematurely' may be found, in the event of relapse or extension of the disease, to be beyond the reach of streptomycin treatment. From the public-health point of view there is clearly a risk of old chronic cases spreading infection with streptomycin-resistant strains, so that patients acquiring meningeal or miliary tuberculosis from them cannot hope, in their turn, to be benefited by streptomycin treatment."

THE BIRMINGHAM HEALTH CENTRE

MOST local health authorities, their housing problems still unsolved, have been only too ready to set aside the provision of health centres as at present impracticable. Where an adequate service (though it may not be a coördinated one) is already provided from doctors' surgeries and municipal clinics, building and other difficulties preclude any ambitious schemes for the improvement of medical facilities. But where districts are inadequately served, or are outgrowing their existing services, new arrangements have somehow to be made, either by communal planning or haphazardly (as in the past) by allowing doctors migrating to the district to find or build accommodation for themselves. Two of our most influential public authorities, in London and in Birmingham, both concerned with the provision of new housing estates, have decided to make the health centre the key to the medical services for their growing communities. The London County Council has approved the building of a health centre on its new estate at Woodberry Down, Stoke Newington, and the Birmingham city council has sanctioned a centre at Stechford.

In some ways the Birmingham project has the greater immediate interest, for it has been planned for construction as a single-story building built from standard prefabricated units. Materials are available for the building and little skilled labour is required for its erection. It should then be possible for it to be built and brought into commission with little delay and so provide a valuable testing ground for group medical practice. If, too, the prefabricated buildings prove satisfactory, the plans and layout of the Birmingham experimental centre may well be copied with modifications wherever a suitable site of sufficient size is available. Single-story buildings admittedly demand sites which in urban areas seem of wasteful size, but in years to come, when more permanent buildings come to be built, we may well be grateful not to have to fit them into inconveniently cramped sites. It is to be hoped, therefore, that when the Birmingham centre is built it will attract many municipal inquirers and not a few imitators.

The centre will serve some 20,000 people. The Stechford site, of about two acres, is easily accessible by buses and cars. The centre will be built of Orlit prefabricated units, around three sides of a square enclosing a forecourt open on the fourth side. It will be finished externally in cream roughcast, and internally in flat oil paint in pastel shades. Decorative schemes in the general-practitioners' suites will vary, and consideration will be given to the doctors' individual taste and requirements. These suites, six in number, will (with a minor-operation room, a recovery-room, nurses' room, office, records-room, dispensary, and laboratory) occupy one wing of the centre. Each suite will consist of a consulting-room, an examination-room, and a waiting-room. The central block will house clinics for maternity and child-welfare services and will include a lecture-hall, a toddlers' nursery and playground, accommodation for sunlight treatment, and a pram-park. The remaining wing has a dental clinic, accommodating two dental surgeons, a caretaker's flat, and the common-rooms for the staff of the centre. These consist of a doctors' common-room, a medical library, a staff common-room, staff dining-room and kitchen, and a suite comprising a bed-sitting room and bathroom for the doctor on duty.

Architect's drawings of the proposed centre have appeared in the Birmingham press, and a detailed plan was published in the *Medical Officer* for Aug. 14 (p. 69). From these it can be seen that the design, which is the work of Mr. Donald A. Goldfinch, architect to the city of Birmingham health committee, is both functionally sound and architecturally attractive. It is a plan, too, which if successful in Birmingham could easily be changed—by alteration in grouping or internal division of its component units—to suit larger or smaller communities or other sites.

Digitized by Google

For the successful building and establishment of a health centre, agreement and coöperation are needed between the health authority, the executive council, and the local doctors. Such agreement, we understand, has been achieved in Birmingham. The plans originating with the health authority (the Birmingham city council) have been approved by both the executive council and the local medical committee. Both these latter bodies are anxious to see the centre built as soon as possible, and they are willing to coöperate fully in arranging for the medical staffing of the centre. The number of local doctors who have already expressed their willingness (subject to satisfactory negotiation with the Ministry of Health as to conditions and terms of service) to work in the centre when it is built is sufficient for the city council to embark without qualms on their project as soon as the sanction of the central authorities has been secured.

This considerable progress makes all the more regrettable the controversy which has arisen, and is still unresolved, between the sponsors of the centre and the Ministry of Health over the potential use of the health centre by private patients as well as health-service patients.

Disabilities

12. BLINDNESS

IN June, 1944, at the age of 30, I was totally blinded by a flying bomb, also receiving multiple injuries to my face, chest, and arms. I had been married for four years, and had a baby daughter of nine months. After four months I was discharged from hospital and began training at St. Dunstan's. I left the training centre in July, 1945, and in the following September started employment with a large firm in the Midlands.

I did not lose consciousness immediately on being hit, and I tried to see what had happened to the other occupant of the room. I couldn't, and therefore experienced my first fear that I had lost my sight. I had my fears confirmed in hospital, when the surgeon told me that he had removed my right eye, and that it was unlikely that the other would ever be anything more than ornamental. There was a remote hope that some sight might return to my one eye, but I never really counted on it, although I secretly tried all sorts of experiments on myself, such as trying to discover whether I could see by shining a torch under the bedclothes. The net result was that I knew the worst very early on.

I cannot deny that the realisation hurt like hell at times, and that I had my periods of intense depression, when everything worth while seemed lost. It hurt to think that I should never again see my wife or my baby daughter, of whom I had seen so little during the war years. Looking back, two principal things helped me to fight off, and avoid showing, this depression—the unfailing courage of my wife, who from the first showed that I should not have to carry my burden alone, and my own determination not to be a burden to others.

My wife was at my bedside when I recovered consciousness in hospital the morning after I was hit. Her readiness to face the future cheerfully was an immense help in determining my own reactions to my changed circumstances. We weighed up our assets and decided that we could still make a success of life. We agreed to present a cheerful face to the world and help each other in doing so.

Stimulated by the cheerful banter of a fellow officer in the next bed, I soon started to do things for myself. I found I could light a cigarette by sliding my thumb along and feeling for the end with a lighted match, though I had an unreasonable fear that I would burn my face or damage my bandaged eyes. I signed all the letters written for me by my friend. With a tremendous effort I wrote a letter in longhand to my wife. I began to form habits to make life easier—to put round things down where they wouldn't roll away, to remember where I had put such things as my razor and shaving soap—and I also began to take a more intelligent interest in things around me. I got people to describe the hospital and the surrounding district. Thus I built up my own mental picture. I learned how necessary it was for sighted people to be accurate in their descriptions; slipshod ones were worse than none at all.

Some things I had to learn by painful experience. A collision with the corner of the bed when I was picking up a shoe taught me that it is advisable to ensure that there is nothing in the way before bending down quickly. My first solo journey on a bus at this time taught me that it is as well to make sure that no-one is occupying the seat on which one proposes to sit. I landed on the lap of a young lady, who fortunately did not take too serious a view of the incident. An embarrassing moment when I tipped the contents of my plate on to my lap brought home to me that a blind person must constantly guard against the tendency to pull the food on his plate towards him during a meal. With my sighted intimates I adopted a system by which they said "six o'clock" if I was in danger of pulling the food off the near edge of my plate. At first I used to get them to describe, as though they were describing a target, the location of food on my plate. "Six o'clock beef, nine o'clock potatoes," and so on. Later I found this unnecessary, though this mode of locating things is useful generally at table. I do, however, like to be told what food is placed in front of me. Some blind people like to have their meat cut up, but I prefer mine served in the ordinary way, even though this sometimes presents difficulties. It was some time before I appreciated that the safest way of approaching one's glass was from above with the fingers slightly extended.

In hospital, I learnt to use my ears more acutely, to use sounds to help me build up my picture of the things round me and so to establish landmarks for finding my way about. Later, when I became more competent in walking about on my own, I began to distinguish the subtleties of echoes thrown back by lamp-posts, walls, and other objects. It was a great thrill when one day I thought I detected a difference in sound indicating that there was an object on my left. I investigated with my stick, and was jubilant to find that there was, indeed, a pillar-box there. I also learnt other devices for getting round on one's own: using the camber to walk along a quiet road, the value of counting one's paces, how to tell the proximity of objects by the difference in air-pressure, and the wisdom of taking a complete turn round a corner before attempting to cross a road, so as not to wander into the middle of a cross-road.

I had been taken under the wing of St. Dunstan's three weeks after being hit. The attitude of my fellow St. Dunstaners was a fine stimulus. They had no sympathy for themselves, reserving their sympathy for other patients in the hospital. With them, in hospital, I learnt to type and read Braille. I experienced an awful fear that I should never develop my sense of touch. For a short time I was horrified to find that I could not distinguish the Braille formations, but the thought that this was the only way out of illiteracy kept me going. Soon I was happy to find that I could read again. Later, I did carpentry, learnt Braille shorthand, played the piano, went horse-riding, and took part in athletics.

One of the biggest problems has been how to adjust one's relations with sighted people. This was particularly difficult in the early stages, when I longed to do things on my own, and well-intentioned but misguided people would try to help me. Once I had acquired confidence in finding my way about I was glad to welcome assistance. Sighted people can be particularly helpful by guiding one in the correct way. I personally dislike being propelled

Digitized by Google

by the shoulders. I prefer to take the arm of the person guiding, so that I am slightly behind him; this makes it easier to avoid obstacles and to be ready for steps up or down. When being shown a chair I like to have my hand placed on its back. In conversation I deprecate the avoidance of words such as "see" and "look."

Apparatus which has been invaluable to me in my job has been a typewriter, Braille shorthand machine, pocket Braille frame for making memo notes, a Braille writing machine, a stock of thin cards about 5 inches by 2 inches, Braille watch, and, of course, my walking-stick. The cards are used for making Braille notes on the pocket frame or for making longhand notes with a pen or pencil. I use a ball-pointed pen so that there is no need to discover which way round to hold it.

Some blind people do not try to keep up their longhand writing. This seems to me a pity. I have managed to continue to write as automatically as I did when I was sighted, and I have found this, and similar operations such as playing a piece of music which one has memorised, fairly easy if one does not consciously think about the operation.

Performing actions naturally, as one did when sighted, is an aim that I have tried to follow in as many directions as possible. Thus, unless there is need for special care, I prefer to walk along using my walking-stick as a sighted person would, swinging it to the right or left if necessary to maintain contact with a wall or grass verge.

* * *

It may seem that I have minimised the difficulties. These have, of course, been perpetual, and some phases have been harder than others. Periods of insomnia have coincided with periods when I was making the greatest effort. At times I have felt the need to relax and be content to sit and do nothing.

My work and my family have not given me much leisure time. The leisure activities of blind people can be legion, so I will mention only the more unusual forms I have sampled. These include high diving, surf-riding on the Cornish coast, aquaplaning, and attempts at playing billiards, snooker, and table-tennis. The last three were failures, but the attempts were amusing.

One of the compensations of blindness is finding ways of overcoming it. Using a dial telephone was at first a laborious process, until I found that all four fingers of the right hand could be employed to facilitate the operation. An aluminium frame, with appropriate spaces, enables me to make out my own cheques. The difficulty of distinguishing between a ten shilling and a pound note was overcome when I found that one could measure the width of the note unobtrusively by passing it between the first and second fingers.

It was some time before I plucked up courage to help my wife with the children—now a girl of 5 years and a boy of 20 months. One has to maintain a hundred per cent. concentration and one must be sure of one's terrain. It is advisable to take some special precautions—to approach a child with one's fingers curled, to back through a doorway when carrying a child, to hold on to the bannisters firmly with one hand when carrying the infant downstairs—but the result is a tremendous gain to any blind man who is fond of children. Ingenuity is needed to devise ways of playing with children, and one has to be constantly on the alert, but the blind man can tell stories with the rest, he can make models in wood or cardboard using his sense of touch to guide him, and many other things besides.

To summarise, I would say that the first essential is to accept cheerfully your changed position. Milton was a striking lesson in this, and many would find his "Sonnet on my Blindness" as helpful as I did. The next thing is to regard yourself as a normal person with extra difficulties and persuade others to accept you as such. The rest is patience, perseverance, and a sense of humour.

In England Now

A Running Commentary by Peripatetic Correspondents

THE boarding-house abutted on a triangle of common, and it was when I chanced to look out of the bedroom window towards the edge of this that I saw the patient. His handcart was abandoned by the roadside, and he, all but his upper end which I could not see for grass and nettles, was twitching violently. His boots were describing circles in opposite directions. Now and then the tonic phase would succeed the clonic.

It is all very jolly to rush out and administer treatment—all very jolly, that is, if you qualified last week. But other things weigh in the mind against a Hippocratic rush to stick one's neck out—inquests two hundred miles from one's home town, persistent beggars complete with hysterical fit, epileptics who prefer to be left to fit in peace or who become pugilistic on recovering consciousness. But I had signed the visitor's book rather lavishly, and everyone looked at me. "There's a man having a *fit*," they muttered in my direction. I went out.

The patient was lying full length in the grass with his head and shoulders down a manhole, struggling with a tap. He met my gaze with an even stonier one, and remarked that someone had fixed down this illegitimate with a sanguinary monkey wrench. Anyhow, the differential diagnosis on the way out had done me good.

* * *

My son, who is half way through his hospital work at his medical school, says in his last letter:

> "I didn't know that I had given you the impression that I was getting slack about work. The truth is that I have been completely 'had' about what our clinical teachers are supposed to do. I had expected that they would tell us what to learn and how to use our knowledge when it was learnt. Instead, each of them presents us with a single piece of a jig-saw puzzle, and leaves it to us to build up the puzzle. It is just too bad if they give us less than half the pieces, and some of them badly cut.
>
> "I have now reached the same place that all students seem to get to at about the same time. We realise that no-one is going to give us a comprehensive picture of the subject and that the only thing to do is to plunge into the books, find the missing pieces, and then try to put them together, still not knowing what the puzzle will look like when completed. It is a shocking waste of time, energy, and money."

The fact is that medicine is one and indivisible. The ophthalmologist may have the first clue to kidney disease, the dermatologist to thyroid trouble, and the symptom of enuresis in a child may disclose a diabetes. It seems to me foolish to stuff students with a modicum of chemistry, physic, biology, anatomy, and physiology and then consider that he is scientifically equipped to deal with medicine.

* * *

Our radiologist is normally a cheerful fellow at luncheon, but today he was prodding his fried spam in a moody sort of way and muttering various letters of the alphabet to himself. We tried to cheer him up, but all he would say was F.H.N.H. ? I.U.D. At first we thought it was some sort of spell to make him see better in the dark but at last we got out of him that he was suffering from acute abbreviophobia, and that he had found the letters written on an X-ray request form that morning. He had no idea what part of the body to X ray. We tried to be helpful: "Fractured Hand Now Hurting? Is Unciform Decalcified" seemed ingenious but unlikely. "Four Horrible Nasal Hæmorrhages ? Investigate Underlying Disease" suggested that a film of the naso-pharyngeal tract should be taken. Eventually, because the request had come from a maternity ward, it was referred to an obstetrician, who decoded it promptly: "Fœtal Heart Not Heard. ? Intra-Uterine Death."

I think the radiologist was right to be annoyed. The amount of irritation or confusion abbreviations cause is greater than the time they save. They can be dangerous too. I have seen a nurse reading "guttæ H & C" and preparing to put alternately hot and cold drops into the eye. I have seen a patient with a sprained ankle on whose card was inscribed T.C.A. (2) having this comfortingly

Digitized by Google

interpreted by a fellow outpatient as "Double Tuberculous Consumption of the Ankle" (though it only meant "To come again in two days").

Most abbreviations are unnecessary: thus, if a patient's father is well it takes ten letters to write "father well" and eleven letters and two stops to write "father a. and w.;" yet every student prefers the latter form. (Surely if somebody is well we can take it they are alive.) Probably the worst offenders are chest experts, with their P.P.'s, A.P.'s, and P.C.'s, expressions which they use in speech as well as when writing. Ophthalmic surgeons are pretty bad too, and I remember one who wrote his opinions on my cases almost entirely in single letters of the alphabet. I cured him by sending him a request P.W.Y.T.M.I.T.P.N.G. (Please will you tell me if this patient needs glasses).

There is one kind of abbreviation which I think *could* be used a lot more. I mean the word made of initials, so much used in the war (PLUTO=Pipe lines under the ocean and FIDO=Fog, intensive dispersal of). In medicine we have only two of this kind—EUSOL standing for Edinburgh University Solution, and BIPP for Bismuth, Iodoform, and Paraffin Paste. May I suggest (neurologists please note) getting rid of dysdiadokokinesia and having DITHER (Difficulty In Twisting Hands Equally Rapidly).

* * *

*On reading Professor Kinsey's survey of Sexual Behavior in the Human Male.**

O cupid! Cast away your bow and quiver—
Statistics prove your method inexact.
O Donne! Go take a jump into the river:
You hymned the essence, but ignored the fact.

Locked in some cool aseptic heaven above,
Trained statisticians painlessly inquire
Into the quaint geometry of love,
The quantitative aspects of desire;
Observe the conduct of the lovesick male
(Not passionate, not noble, not obscene),
And plot it on a logarithmic scale,
Noting a random scatter round the mean.

O monumental volume, smug and fat!
Did Man, who wrote the Song of Songs, write that?
O God! O Kinsey! O Jehoshaphat.

* * *

Please sir, I want to patent a smile. You know that chap Parkinson, who patented the mask? Well, in the same conditions in which you get that bland or sometimes almost brutal lack of expression you get a most glorious smile. It's like the sun breaking through thunder clouds, or ham and eggs when the dish-cover is removed, or better still like a child's face watching a clown. Scientists would probably describe it as having a heavy geniality content or a high coefficient of friendliness. I want it called a Percy Peripat's smile. Perhaps someday people will say of a book or a play, "It's a perfect Percy Peripat——."

Poor Parkinson, but perhaps he was modest like Linnæus, who had only a weed named after him when he might have had something grand like an orchid or lovable like an oxlip.

* * *

Mrs. J induced abortion on herself and because of continued bleeding a D and C was done and two further fœtuses removed. When she was informed later that she had had triplets her comment was: "But doctor in that case you should have left the other two because if I had twins I would be a top priority for a prefab." There is a great deal in this Social Medicine that we doctors do not appreciate.

* * *

At a conference the surgeon replied to a physician's query: "I am sure DR. X knows as well as I do how to treat these cases—one should abandon the A.P. and buy some streptomycin in the black market." At this conference, also, I was encouraged to hear a tuberculosis administrator say that the trouble is that we have a state of inflation, with too much paper chasing too few beds.

* Before jumping to conclusions from these lines, students of sexual behaviour should see our review of this book (*Lancet*, 1948, i, 795) or, better still, the book itself.—ED. L.

Letters to the Editor

STUDENT SELECTION

SIR,—The rush to join the medical profession has created for the psychologists a problem which on their own admission will keep them pleasantly occupied for many years to come, and which will no doubt provide jobs at the public expense for many recruits to their ranks. This new research will, it can be confidently predicted, go the way of all other research, spreading in endless ramifications and never reaching finality. Already there is adumbrated the first extension—research into the selection of people suitable for the selection of people suitable for the pursuit of medicine. And so it will go on and on. The possibility of raising the percentage of "outstanding" students from 10 to 39, envisaged by Mrs. Petrie (Aug. 28), illustrates the lack of logic which characterises many of the emanations from our laboratories. For when 39% are outstanding against 61%, it will be our proud boast that never were so many outstanding against so few. The problem will be solved, not by the tests, matrices, and screenings of the psychologists, but by the study and correction, by minds untrammelled by the jargon of modern science, of the motives behind the abnormal desire for entry. The chief of these motives are four: snobbishness, the lowering of financial barriers, the call of idealism, and the search for economic security.

In regard to the first and second, the easier the climb, the greater the number of climbers; we can only hope that the creation of new hills will ease the congestion on our own. To the idealism of adolescence medicine presents an appeal which is lacking in all other vocations except the Church. The doctor is noble and self-sacrificing, a beacon of virtue in this sinful world. In contrast, the business man is selfish and avaricious, flourishing on the exploitation of his fellow men. A young man just down from Oxford told me with great joy that he had obtained a post in hospital administration. "There," he said, "I shall be doing good in the world. If I had gone into industry I should only have been making money selfishly. I could never have stood it." His attitude shocked me, for I thought his university would have taught him better. It is, however, a view which is widely held. The inevitability of the association of trade with social injustice is a doctrine which dies hard, being perpetually fanned into flame by many of our sociologists, who keep harping on the evils of the industrial revolution. The headmaster of one of our leading public schools tells me that there are twice as many boys leaving to take up medicine as there are doctors' sons. Many of them embrace medicine scorning the family businesses where they are sorely needed.

To many parents financial security is a prime inducement. After all, the sick will always be with us whatever happens. These people do not realise that prosperity in medicine depends entirely on the prosperity of our export trade. There can be no security in medicine unless that trade is secure. We ought to view with grave concern the prospect of the most intelligent of our youth being encouraged to shun commerce as something unsafe and unclean, and to seek financial security and moral salvation in a profession completely dependent on commerce. We may question whether the attempt to cream off the ablest into medicine is in the highest national interest.

We must learn to see medicine and the community in their proper perspective. We must realise that, intelligence being limited in quantity, medicine cannot be enriched without the impoverishment of other vocations where it is needed just as much. We must educate youth and parents in a saner, more realistic, and less sentimental outlook. The headmaster mentioned above, seeing the danger with a prescience unfortunately lacking in the leaders of our profession, has shown the way. He has instituted lectures by men prominent in agriculture and industry with the object of teaching boys that in those fields there are opportunities for the cultivation of moral and intellectual qualities as great as or even greater than those existing in medicine.

Digitized by Google

We shall solve the problem only if we discard the narrow professional for the broad national point of view, bearing constantly in mind that our future prosperity depends on the attainment of a balanced society.

Cambridge. FF. ROBERTS.

SIR,—Your extract [1] from the paper by Dr. Fraser Roberts and Dr. Eliot Slater is wisely chosen. As a signature tune to the main subject of your educational number for 1948, might it not be rewritten thus:

> "Few would deny the advantage of a well-stored brain, a high power to correlate clinical observations with interrogation and laboratory reports, and to devise further investigations, an impressive manner, clear speech, and a good enunciation. Such qualities entitle their owner to submit his name for fellowships or clinical appointments at our teaching schools; but for the doctor, whoever and wherever he be, our aims are much less clear. There is needed a kindly heart, a gentle touch, the control to keep a confidence, love of children, with the power to make a decision and to accept responsibility."

Without these he is nothing. An experience of 38 years in trying to choose the best men for appointments at the end of their student career has shown the difficulty of selection by whatever means. Nor does psychology as yet offer any way whereby the desired characteristics may be foreseen five to seven years before they have to come together into action.

These younger men that today have in their hands the selection of medical students have indeed a hard task. But have they envisaged all that means? By the time we have responded to Wilfred Trotter's teaching that "it is no longer possible to conceal the wholly unique importance of medicine for the very existence of social life," I estimate the profession must be doubled. It is therefore not a problem of cutting down the numbers to those that the medical schools can hold, but of expanding the medical schools in size and number to take three or four times as many students as today until that number has been reached, and then stabilising them at double. Although the Barlow Report on Scientific Man-power did not specifically refer to medicine, the principles there laid down apply to us as much as to the qualified scientists with which it deals.

So far as I can see nothing has been done, as yet, in any way to attempt to tackle the problems of that report; and yet our continued existence as a nation must depend upon our efforts to do so as much as upon workers in mines, factories, and fields to increase production.

London, W.1. T. B. LAYTON.

BINOCULAR MICROSCOPES

SIR,—Dr. Shackle's letter of Aug. 14 is full of interesting observations, on which I have a few comments to make. But I would like to state clearly that what I am putting forward are only views and not carefully ascertained experimental facts.

The first important point is that whereas it is not tiring to use relaxed accommodation and parallel optic axes, or to use accommodation for 10 in. distance and convergence for 10 in. distance, it is also not fatiguing as a rule to change from one to the other. In other words, the idea that converging the eye axes after they have been rendered parallel, or vice versa, causes fatigue is, I think, wrong. The muscles are usually fully able to carry out these functions; presumably this is due to reciprocal innervation, which enables a muscle attached to one side of the eye to contract at the same time as its antagonist attached to the other side of the eyeball relaxes. The same statement applies to accommodation—that accommodation as such, from distant to near vision, or from near to distant vision, does not as a rule cause noticeable fatigue. What does cause fatigue is the necessity to accommodate for one distance and to adjust the eye axes for a different distance; and what is certainly in my case far more fatiguing still is the need for causing one field to be raised or lowered in respect of the other, to enable binocular fusion to take place. Whenever, therefore, I have experienced fatigue in using a binocular instrument it has been the vertical alignment which I have always scrutinised. I wonder if this is the cause of the discomfort that Dr. Shackle has experienced with the converging type of microscope, which he mentions in his letter? He might try putting prisms of small angle, base-down or base-up, between one of the eyepieces of this instrument and his eye, to see if this causes an improvement.

To summarise: I cannot see any fundamental reason why the parallel type of microscope is superior or inferior to the converging type. It may well be, however, that one observer will have a personal preference for one rather than the other. If, having purchased one type, it is decided after further trials that the other type would have been preferable, all that need be done is to place suitable prisms above the tops of the eyepieces. For the best results, these prisms should, of course, be achromatic.

H. HARTRIDGE
Institute of Ophthalmology, London, W.C.1. Director, Vision Research Unit, Medical Research Council.

PLANTAR WARTS IN SCHOOL-CHILDREN

SIR,—In 1947, at Walthamstow, 94 girls and 56 boys with plantar warts were referred for treatment through the school health service. Since the facilities for treating this and other foot conditions are widely known in this borough, this figure of 150 cases can be taken as a fair indication of the incidence of plantar warts in a school population of 16,463. The monthly rates were: January, 13; February, 11; March, 7; April, 13; May, 10; June, 8; July, 7; August, 1; September, 22; October, 21; November, 21; and December, 16. The low incidence in August is of no significance, for attendances at all clinics during school holidays fall off considerably, but the slight rise in the next three months may have resulted from increased activities, especially swimming, during the summer months. The incidence for the year in age-groups was: infants (aged 5–7) 7%; juniors (aged 7–11) 27%; and seniors (aged 11–15) 66%. The increased incidence in the 11–15 age-group is probably due to increased participation in physical training, swimming, dancing, &c.

The right and left feet were equally affected. Most of the patients had one wart only; 11 had multiple warts on one foot, and 12 had multiple warts on both feet; 80% of the warts were in the plantar metatarsal area and anteriorly, and 20% on the heels, the large majority being situated on pressure points. Outside this series only one has been encountered on the protected area afforded by the longitudinal arch.

Treatment was carried out entirely by registered medical auxiliary chiropodists in the municipal foot clinic. The standard treatment, adopted in most cases, was as follows:

(1) Swabbing of the whole foot with surgical spirit.

(2) Removal of any mass of callous tissue to facilitate the action of the acid to be applied.

(3) The area surrounding the wart is painted with collodion or with tinct. benzoin. co. to prevent irritation by zinc-oxide plaster.

(4) The wart is isolated with a stockinette cover in which a small hole is cut about the size of the wart.

(5) 'Chlorosal' (salicylic acid 60%, chloral hydrate 5%) is applied through the hole in the stockinette, and a felt pad, cut so that no direct pressure results, is placed over the wart.

(6) The whole dressing is finally enclosed in stockinette and secured with adhesive strapping.

The patient is instructed to keep the wart dry and to return in 7–14 days, when the treatment is repeated. The above-mentioned procedure takes 6–8 min. for each wart. On the average three treatments only are necessary but two subsequent visits at monthly intervals are insisted on for checking the results. Monochloracetic acid and silver nitrate are occasionally used instead of chlorosal. This treatment is painless in most cases, and where pain is experienced it passes off very quickly. The average number of attendances before final discharge was 5·6, and the average number of treatments 3·8.

The results of treatment were assessed in 59 children who had completed their treatment not less than nine months previously. All these children were taken at

1. *Lancet*, Sept. 4, p. 377.

Digitized by Google

random from the higher age-group, because they could give more reliable answers to questions. In no case was there a recurrence, and only 4 children showed any signs of the location of the warts; these were in the form of small localised callosities. Indeed most of the children had forgotten the site of the warts, and several did not know which foot. Advantage was taken at this examination of noting any associated foot abnormality. Slight pes planus was found in 2 cases, and a moderate degree of hallux valgus in 6, but the position of the warts in these cases could not be associated with the deformities.

Of these children 36 used the swimming-baths all the year round, and 15 in summer only; 39 used shower-baths regularly after physical training. Only 2 had used communal gym.-shoes.

Of the many hundred cases treated before at the foot clinic none have had to be referred for more energetic measures.

Without precise knowledge of the ætiology of plantar warts, preventive measures are mainly directed towards excluding established cases from places which favour the spread of this disease—i.e., swimming-baths and showers. The feet of children using such places should be frequently examined. It is doubtful whether the use of disinfectants for the surrounds of baths and showers is of any value. In many affected children a primary stimulus, probably an abrasion, may have been produced by nails jutting into the shoe or by ill-fitting shoes. It is therefore important that shoes should be properly fitted and comfortable.

Our experience shows that (1) conservative treatment is eminently suitable for plantar warts and is the method of choice for school-children; (2) chiropodists are competent to deal with this condition, thus doing away with the need for surgery under anæsthesia which wastes medical man-power; (3) other forms of treatment expose the patient to risk of scarring and ulceration on pressure points; (4) little or no discomfort and very little limitation of activities result from conservative treatment; and (5) the expenditure of time and money compares very favourably with that in other forms of treatment.

I am indebted to Dr. A. T. W. Powell, M.O.H., Walthamstow, for his permission to publish these facts.

MELVILLE WATKINS
Walthamstow. Deputy Medical Officer of Health.

SHOULDER-GIRDLE SYNDROME

SIR,—In their article on June 26 Dr. Parsonage and Dr. Aldren Turner did not mention syphilitic amyotrophy in their differential diagnosis. In view of this the following case may be of interest.

A miner, aged 47, reported to the medical outpatients' department on July 27 with a history of being perfectly well until 10 days previously when he was suddenly seized by a sharp pain in the right shoulder, while sitting at home. The pain increased, reaching its maximum intensity in 48 hours and making sleep impossible. It then spread to the neck and outer border of the upper arm as far as the elbow; it was slightly aggravated by movements of the shoulder, but eased by supporting the arm in a sling. Then, 4 days after the onset of pain, he noticed some weakness of the arm which gradually increased during the next week. There was no recent history of trauma, malaise, headache, visual upset, or paræsthesiæ.

Examination showed slight wasting of the right deltoid with marked weakness of abduction, although all movements at the shoulder were restricted owing to the severe pain. The biceps and radial reflexes on that side were diminished, but the triceps reflex was brisk. Sensation was unimpaired and no other abnormalities were found in the central nervous system. The heart was moderately enlarged, and there was a diastolic murmur in the aortic area; X-ray examination of the chest showed generalised cardiac enlargement with dilatation of the aorta. Blood Wassermann reaction (W.R.) was negative.

The patient was admitted to hospital on Aug. 16. The wasting of the right deltoid had increased and the right supraspinatus and infraspinatus were also involved; the pain, however, was reduced to a dull ache and sensation remained normal. Blood W.R. was still negative; but the cerebrospinal fluid contained 50 mg. protein per 100 ml., and 30 cells per 100 c.mm., and the W.R. was strongly positive.

This patient's symptoms and signs closely resemble those of the shoulder-girdle syndrome, and had not the condition of the heart directed our attention to a possible syphilitic ætiology the patient might not have been admitted for lumbar puncture; and thus the correct diagnosis would not have been reached.

CHALMERS H. DAVIDSON
Royal Infirmary, Edinburgh. NEIL S. GORDON.

CONTRACEPTION IN GERMANY

SIR,—At the Cheltenham Congress on Population and World Resources Dr. Durand-Wever's remarks about contraceptive clinics in Berlin referred only to the Russian Zone. Both from the platform and in private conversation she complained how odd it was that, in the British and American zones, not only were contraceptives forbidden but the passage of appliances and literature through the post was effectively stopped by the Control authorities; and that Allied governments were still continuing the repressive measures against contraception first begun by Hitler. This position is directly related to the figures given, of one abortion for every live birth. It would be unfortunate if your readers were to assume that in this terribly urgent problem freedom to limit the family existed in the British and American zones, where in fact such freedom is most effectively denied.

As one Dutch delegate put it, speaking of the time when, under the Germans, contraception was forbidden in Holland: "They made us contraceptually impotent." It seems a tragedy that in an area containing 65% women, according to Dr. Durand-Wever, and where the need is so urgent, the British authorities should continue the legislation initiated by Hitler.

Urmston, Lancs. B. SANDLER.

FAMILY PERIODIC PARALYSIS

SIR,—In 1901 Sir Farquhar Buzzard[1] gave in your columns an account of this rare disease in two young brothers and their mother. As the younger of the two brothers in this report I should like to describe an accidentally discovered means of alleviating the condition.

The attacks may be divided into two kinds: (1) ordinary, and (2) continuing.

Ordinary attacks are the more frequent, with sometimes as many as four in a day. Two of these would probably be local and very slight, not much more than a feeling. These attacks do not come on during muscular contraction, though the arms may be affected while one is walking. The immediate cause of an attack appears to be anything that lowers the vitality—for instance, exercise, hunger, cold, or diarrhœa. A slight attack may occur locally after the use of certain muscles, perhaps in a hand or arm, or in both hands or arms. A bad attack will affect all the muscles of the body, and a very bad one also affects severely the internal organs. The heart seems to flutter, the eyelids have a tendency to close, the back of the tongue seems to swell (I do not think that it really does), and swallowing and speech become difficult. Sight, hearing, and consciousness are not affected, but the whole of the body is helpless. Such an attack may last for an hour or more. After it is over there is a feeling of great rest and refreshment, and all tiredness felt before the attack came on has gone. Attacks are accompanied by an unpleasant but not painful sensation that I cannot describe; there seems to be a soft grip about it. Occasionally an attack comes on with practically no sensation, or a very slight attack may be accompanied by a lot of feeling. The likelihood of an attack gets less as the day advances, but one may occur in the night during sleep.

Continuing attacks sometimes follow ordinary attacks and are much the more tiring of the two. They may last for some days and are accompanied by a "beaten" feeling in the parts affected. They occur generally in the legs below the knees, either in the muscles in front of both legs or in those at the back of both. In either case walking is very difficult and exhausting.

1. Buzzard, F. E. *Lancet*, 1901, ii, 1564.

Digitized by Google

When one is sitting still and an attack starts to come on, it may be lessened and sometimes kept off by working the muscles. One may get up and walk about or contract and relax the muscles above the knees. This is not always successful with a very bad attack.

In, I think, 1911 I returned from abroad after having had typhoid fever. On my arrival at an English port I had an attack of the continuing paralysis which rendered me almost helpless for three weeks. I think the immediate cause of this particular attack was the strong sea air. We went inland and my father suggested that I should take cod-liver oil to pick me up. After a little time I noticed that almost all attacks of the paralysis had ceased, and my mother and brother therefore started to take the oil and with the same result. The oil is not, however, a cure, but a "keep off" and has to be taken continuously. It takes full effect in about a fortnight, and after it is left off the attacks are in evidence as usual in about the same time. The amount to be taken varies with the amount of exercise one takes and with other circumstances; but, roughly speaking, about 1 pint a week is enough. Less will help, but minor or medium attacks will probably occur. The oil enables one to live a more or less normal life, though of course not a very strenuous one. The continuing attacks never occur when one is taking the oil. When starting to take it, they are the first to go; and they are the last to reappear when it has been left off. In my experience only the pure oil does any good.

G. D. H.

*** Farquhar Buzzard's article provided the first record in Great Britain of periodic paralysis affecting more than one member of a family. In the same year Dr. H. D. Singer had reported a sporadic case in the summer number of *Brain*.—ED. L.

THE CROSSBOW OUTLET PELVIMETER

SIR,—I was interested in the instrument described by Mr. Morris (July 24, p. 139) for the obstetrical evaluation of the pubic arch. Two years ago I devised an instrument for measuring the anterior and posterior sagittal diameters of the outlet and have since used it on some eighty patients with pelvic contraction, who were sent for X-ray pelvimetry.

This outlet pelvimeter is of a crossbow pattern (fig. 1) and is made of brass, which may be sterilised by boiling and kept in 'Dettol' solution. It has three component parts—a half-circle of $3^3/_4$ in. diameter and with a transverse axial bar (which represents a hemi-section of the fully flexed and unmoulded, full-term fœtal head), a T-connecting piece, and a measuring rod. The transverse axial bar of the half-circle is $3^3/_4$ in. long, equivalent to the biparietal diameter of the fœtal head, and is incomplete in the middle to allow the measuring rod to pass as required; and two eminences are raised on the bar which appose the fitted connecting T-piece. The brass circumference is $^1/_{24}$ in. thick and $^1/_8$ in. wide, and has an opening at its apex through which the measuring rod passes. The T-piece is hollow and receives the cut ends of the transverse bar as far as its eminences, and through its vertical part, which is 1 in. long measured from the centre of the transverse axis, passes the measuring rod. A central screw can be tightened to fix the measuring rod.

The measuring rod is 8 in. long and has a curved sacral end to enable the posterior sagittal diameter to be measured; its scale begins at the straight end and finishes at the curve of the rod $1^1/_2$ in. from its tip. The measurement of the anterior sagittal diameter begins at the straight end of the rod, and is read down to the vertical bar of the T-piece, which adds 1 in. to the estimated length.

A measurement is made with the patient in the left lateral position with both thighs fully and equally flexed. The circumference of the pelvimeter approaches the pubic arch from behind and is gently pressed forward against its rami. The measuring rod is then inserted through the brass rim to the apex of the pubic arch, and the distance from the symphysis to the transverse bar is read off. This is considered to be the true anterior sagittal diameter of the pelvic outlet which is being measured, since the available transverse diameter of the outlet occurs where the head will pivot and is positioned by the cross-bar and may be in front of or behind the ischial tuberosities according to the width of the pubic arch.

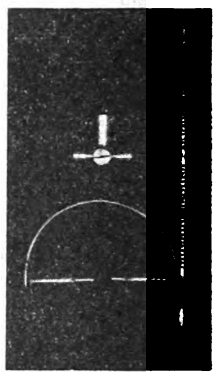


Fig. 1.

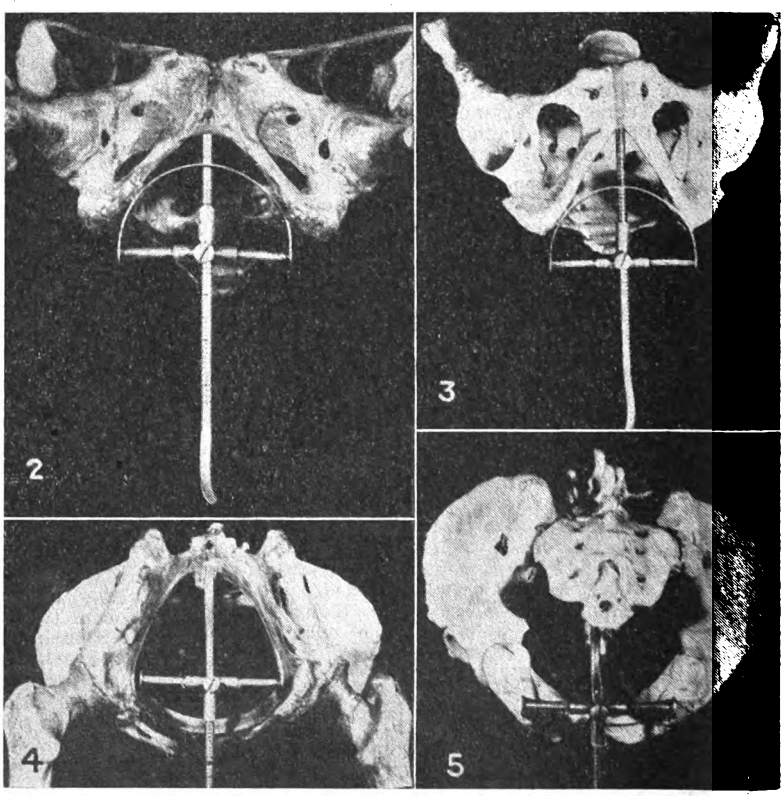
Fig. 2 shows the pelvimeter in position in an average-sized pubic arch, and the anterior sagittal diameter measures 2·6 in.

Fig. 3 shows an anterior sagittal measurement of 3·6 in. in a pelvis with a narrow pubic arch. From an estimation of the anterior sagittal diameter in eighty cases it has been found that measurements above 2·8 in. indicate a narrow pubic arch, and the greater the measurement the narrower the arch.

Without the pelvimeter being moved the posterior sagittal diameter is measured. The measuring rod is withdrawn sufficiently for the T-piece to pivot on the transverse axial bar, and the curved end is swung to touch the outer aspect of the sacro-coccygeal joint, which has been located by moving the coccyx with the fingers, one of which palpates from inside the vagina. This measurement has been shown to average 2·3 in. and to be influenced by the length of the anteroposterior diameter of the outlet and the narrowness of the pubic arch. In fig. 4 the posterior sagittal diameter measures 2·8 in. and in fig. 5 1·4 in.

D. J. MACRAE.

Queen Charlotte's Maternity Hospital, London.



Figs. 2–5.

Digitized by Google

BEDS FOR PULMONARY TUBERCULOSIS

SIR,—The correspondence on this vital subject initiated by Dr. Bentley's article of May 8 and exacerbated by Dr. Stradling's letter (Aug. 21) has caused Dr. Snell and his colleagues (Sept. 4) to touch on the really important and thorny topic of the direct control of beds.

They say: "We do not think the bed position would be greatly improved by giving the chest-clinic physician direct control of all beds." This statement should, I feel, be approved if the sanatorium is to play its proper rôle in the tuberculosis scheme. The sanatorium physician should have a large part in the allocation of cases to the sanatorium under his jurisdiction, if not the final word on their admission. This is not so today. In giving this responsibility to the sanatorium physician three ends would be served: (1) it would help to bridge the gap between the clinic and hospital physicians; (2) it would go far to making the central waiting-list less "central"; and (3) it would ensure that the truly treatable case was seen at an early date by the physician who is to be in the charge of treatment.

"Every sanatorium is good as its medical superintendent," and the enhancement of the authority of the physicians of these institutions would eventually rid the sanatorium of much of its chronic and untreatable population to the benefit of the early case on which alone the best results of treatment, especially chemotherapy, can be realised.

M. M. NAGLEY
Assistant Senior Physician.
Grove Park Hospital,
London, S.E.12.

SUPERNUMERARY NIPPLES

SIR,—I have read with interest the letters following Dr. Harper's paper of June 12 on supernumerary nipples in connexion with neurosis, but I should like to know whether there are any figures for the occurrence of extra nipples in the two sexes. I have never seen supernumerary nipples in a woman, but have seen quite a number in men. Whether this is merely a coincidence I do not know, but I have come to regard this abnormality as commoner in men than in women.

G. DUNDERDALE.
Nanyuki, Kenya Colony.

This letter has been shown to Dr. Harper, who replies as follows.

Dr. Dunderdale, in expressing his belief that polythelia is commoner in men than in women, is in line with the classical opinions of Leichtenstern [1] and Bruce.[2] Of Leichtenstern's own 13 cases, 9 were in men, and 4 in women. However, he extracted from the literature 92 cases, of which 70 were in women, nearly all of whom were pregnant, and only 22 in men.

Bruce records 24 cases, of which 19 were males (9·1% of 207 males examined) and 5 females (4·8% of 104 females examined). Both observers recognise the following sources of error: (1) the variation in characteristics of the groups examined; (2) the greater ease of detection of vestiges at routine examination in male subjects, weighting the scale in their favour; and (3) the special attention directed to the breasts in pregnant women, influencing the scale on behalf of the female sex.

Certain racial differences appear to exist. Among Japanese women 5·19–6%, and among Japanese men 1·68–2·03% are recorded by Iwai. For Chinese men the figure given by Takeya [3] is 3·6%.

de Cholnoky [4] has dealt with the phylogenetic significance of supernumerary breasts, both on and off the embryonic milk line, and believes that polythelia occurs in equal numbers of persons in the two sexes, a conservative estimate being from 1 to 2% of the population. He draws attention to published figures giving the incidence as high as from 14 to 23·3% of the population, but believes his own estimate to be more exact. He has collected from the literature 64 cases of breasts in atypical positions; 37 of these were in women and 27 in men.

My own cases of supernumerary nipples in the embryonic milk line include 72 men and 100 women. However, the preponderance of females at outpatient clinics and surgeries makes these figures of general interest only as regards sex incidence. The paper by Matthews and Baxter [5] deals with the much rarer occurrence of polythelia in subhuman primates. The small number of cases hitherto described include both males and females.

Should we require a reminder of the difficulties of statistical certainty in this field, we may remember these words from Darwin's "Origin of Species": [6]

"Rudimentary organs may be compared with the letters in a word, still retained in the spelling, but become useless in the pronunciation, but which serve as a clue for its derivation."

RICHARD HARPER.
Barnstaple.

1. Leichtenstern. *Virchow's Arch.* 1878, 73, 222.
2. Bruce, M. *J. Anat. Physiol.* 1879, 13, 425.
3. Takeya, S. *J. orient. Med.* 1934, 20, 32.
4. de Cholnoky, T. *Arch. Surg.* 1939, 39, 926.
5. *Proc. zool. Soc.* 1948, 118, 144.
6. Darwin, C. Origin of Species. 6th ed. London, 1895; p. 377.

DIRECT REDUCTION OF FORWARD DISLOCATION OF THE MANDIBLE

SIR,—Though forward dislocation of the lower jaw is not common it is by no means rare, and every general practitioner or casualty officer is likely to be called on to treat it. In this type of dislocation the condyle and the articular disc slip forward into the zygomatic fossa when the mouth is opened too widely. The usual textbook method of reduction is as follows:

The patient sits in a chair, and the surgeon stands in front of him, introduces his well-protected thumbs into the patient's mouth, exerts pressure with the thumbs on the lower molar teeth downwards and backwards to disengage the condyle from the zygomatic fossa, and then with his fingers raises the chin.

In most cases this method is successful and can be performed without anæsthesia. But sometimes the reduction is not easy and the patient suffers agonising pain at each renewed attempt.

The following simple and effective method of reduction, so far as I know, is neither described nor taught in medical schools either in Great Britain or on the Continent. It does not call for anæsthesia, can be executed in half a minute, and is practically painless. The posture of the patient is irrelevant, and the protection of the surgeon's fingers unnecessary. The surgeon introduces his index finger (in bilateral dislocation both index fingers) into the vestibule of the mouth—i.e., between the cheek and the mandible—as far as a point $1^1/_4$ in. above the last lower molar, palpates the coronary process of the mandible (easy to palpate if the jaw is dislocated, but not when the jaw is in its normal position), and presses gently with the tip of his finger on the coronary process backwards and downwards, whereupon the condyle slips back into the mandibular fossa with ease.

This direct method has never yet failed me though I always used it in difficult cases where I was called when the textbook method had failed. Now that the casualty officers have learnt the simple trick they find it just as satisfactory as I have found it.

G. MASCHANZKER.
New York.

SIXTY YEARS OF MEDICAL DEFENCE

SIR,—Your annotation on Aug. 14 put forward some cogent reasons for amalgamation of the two rival defence organisations. It appears that a strong case can be made for "pooling the experience and resources of the existing bodies" at the present time. In addition to the broad issues of policy and finance mentioned in this article there is a further point which may be worth consideration.

My principal and I are severally indebted for quiet sleep during an aggregate of some thirty years to the security afforded by our respective membership of the Medical Protection Society and the Medical Defence Union. Our reasons for joining the rival camps go no further than the individual predilections of the forensic-medicine lecturers at our different medical schools; neither of us is aware of advantages to commend either body in preference to its rival. But being together faced with allegations against our professional conduct, unfounded though we both believe them to be, it seems inefficient as well as irksome to be obliged to lay our common problem separately before two advisory

Digitized by Google

bodies, notwithstanding their equal competence and trustworthiness.

This difficulty of two professional associates together faced with allegations on the same ground by the same patient cannot be unique. Would not the respective councils of the two bodies in which our confidence is placed do well to consider combining not only resources but advisory offices? That this would benefit the members of each by pooling experience and economising administration, is apparent. It would also save the feelings and time of any who may find themselves in the unfortunate position of my senior colleague or myself.

UNIONIST.

THE INTENDING EMIGRANT

SIR,—A peripatetic correspondent of Aug. 21 comments on the lack of preparation of intending emigrants. An Empire information bureau has been established by the Royal Empire Society to answer questions *inter alia* on living conditions in our Empire territories. Information on the very points mentioned—housing, clothes, cars, education—is given freely to all inquirers whether by post or in person. A series of information papers on living conditions has been prepared for seventeen Colonial territories; these can be consulted in many public libraries or can be obtained on application (enclosing postage) to this address.

ARCHER CUST
Secretary-General,
Royal Empire Society.

Northumberland Avenue,
London, W.C.2.

ASSOCIATION OF WHOLE-TIME SALARIED SPECIALISTS

SIR,—Further to the notice in your issue of July 17, (p. 127), the members of this association (formerly the Association of Municipal Specialists) feel that much was done in the past by the old association to secure for them adequate representation on important medicopolitical committees, and valuable advice has been given on salaries, legal problems, &c. This work will be carried on by the new association, whose four principal objects are as follows: (1) to improve the practice of medicine in all its branches; (2) to improve the status and promote the general interest of whole-time salaried specialists; (3) to provide opportunity for discussion on matters of professional interest and policy; and (4) to promote good relations between all specialists.

All whole-time salaried specialists are eligible for membership, and I shall be pleased to supply further information on request.

RUFUS C. THOMAS
Honorary Secretary.

45, Lincoln's Inn Fields,
London, W.C.2.

HOSPITAL LIBRARIES

SIR,—Your annotation last week is a welcome indication to library workers of the increased value placed on the services which they administer. Your advocacy should encourage the new hospital authorities to provide adequate libraries for all kinds of readers—doctors, nurses, and patients—who look to them for books, and to realise the need, which you emphasise, for trained library staff. But your suggestion that the scientific and recreational libraries in hospitals should be combined is open to question. A committee appointed by the Library Association to consider the training of hospital librarians resolved in 1945 that these two categories of hospital library are incompatible. As you point out, it has been proved that recreational libraries are often best administered by the local public library. But the scientific literature required by the professional staff and auxiliaries, by the practitioners of the district, and by medical students must be dealt with, as the Library Association's committee agreed, by a distinct and specially trained staff.

W. R. LEFANU
Librarian,
Royal College of Surgeons of England.

London, W.C.2.

SIR,—The recognition in your annotation last week of the contributions of voluntary work in libraries for patients, is most encouraging to members of the Guild of Hospital Librarians. Our special aim is to contribute to the welfare of patients by loyal attachment to the hospital, and by increasing our own efficiency. The publication of a quarterly periodical, the *Book Trolley*, forms a bond of union and interchange of experience. More could be done by the guild with an increase of membership, and we should welcome the coöperation of your readers in attaining that object.

MARY BUCHANAN
Chairman of the Guild of
Hospital Librarians.

102, Carrington House,
Hertford Street, London, W.1.

THE DEAF CHILD

SIR,—In the article on this subject (June 12) in your disabilities series I was surprised to see no mention of the school medical officer. Surely he is the man to put parents on the track of obtaining help in such a case. Under the new Act the child does not need to be on the books of a school to be eligible. Furthermore, the writer's remarks about war-time London were not strictly accurate. There was at least one school for the deaf open; its name escapes me at the moment, but it was situated just to the south of Victoria station—a school so noisy owing to the proximity of the trains that only deaf children could possibly use it.

W. NORMAN TAYLOR.

Fort Hare, Cape Province,
South Africa.

SHOULDER PAIN FROM PEPTIC PERFORATION

SIR,—The occurrence of shoulder pain in peptic perforation is widely recognised as evidence of diaphragmatic irritation. The pain is generally felt on the right side but may be bilateral, in which latter event it is suggested that anterior perforation is causing irritation of the median portion of the diaphragm.[1]

I recently operated upon a man for perforation of a gastric ulcer into the lesser sac. The usual signs and symptoms were present, but, in addition, he had pain in the *left* shoulder commencing at the same time as the generalised abdominal pain; this was presumably due to irritation of the left half of the diaphragm.

Most anatomy textbooks indicate only a limited relationship of the lesser sac to the crura of the diaphragm—chiefly of the upper recess with the right crus. Crymble,[2] in *Quain's Anatomy*, deals in more detail with the anatomy and variations of the lesser sac. The bursa omenti minoris communicates on the left with the bursa omenti majoris through the variable-sized foramen bursæ omenti majoris. This latter bursa is itself subdivided into an upper and lower portion by the plica cardiaca. It is this upper part which comes into relationship with the left crus and lower posterior portions of the diaphragm.

Lesser-sac perforations are uncommon, and I would hesitate to draw conclusions on observation of only one patient; but it would be interesting to know if other surgeons have noticed left-sided shoulder pain in similar cases.

C. PATRICK SAMES.

St. Mary's Hospital, London, W.2.

M.R.C.P. EXAMINATION

SIR,—I have read the correspondence on this subject with interest, since I passed only at the fifth attempt; and I should like to supplement the criticisms of your correspondents.

At my first attempt, in which I survived the clinical part, I was told to look at a "short case" which the examiner informed me was cardiological. It proved to be one of obstruction of the vena cava secondary to carcinoma of the lung: the patient certainly had signs which might be mistaken for cardiac failure, but the examiner agreed that there was nothing wrong with the heart, over which I had naturally puzzled for some time. On another occasion I was given a man with G.P.I. who refused to answer any questions whatever. On a third I was shown a man with syringomyelia who was stone deaf: if one pricked him with a pin he would say "sharp" or "blunt," but he had no other conversation. The time that I passed, I had perfectly straightforward cases, none of the patients being psychotic or deaf or otherwise debarred from giving a history.

1. Cope, V. Z. Early Diagnosis of Acute Abdomen, 9th ed. London, 1946; p. 102.
2. Crymble, P. T. Quain's Elements of Anatomy, 11th ed., vol 2, pt. 2. London, 1914; pp. 345, 354.

Digitized by Google

No doubt examiners take these factors into account; but the psychological effect of being deliberately misled or faced with a patient who cannot coöperate is devastating. From my experience I would say that the examination is an extremely poor method of differentiating those who have a wide knowledge of clinical medicine from those who have not; and that the conditions are so radically different from those obtaining in an outpatient department or ward that not even the most experienced examiner can detect which candidates are likely to excel in these fields. The art of taking a history is at least as important as the ability to elicit physical signs, and the former is scarcely tested at all in this examination.

I myself lay no claim to a particularly detailed knowledge of general medicine; I took the examination in order to specialise; however, several of my friends whose experience and knowledge in this field far exceed my own, and whose advice I often seek, have so far been unable to pass the examination. I would agree with "Would-be-Member" (Aug. 21) that the only solution is to increase the time spent on the clinical portion, and if possible to see the candidate at work in an outpatient department. This would no doubt make the examination even more tedious and expensive, but it might ensure that this overrated title of M.R.C.P. was conferred only on those who deserved it.

FORTUNATUS.

URINARY INCONTINENCE IN THE AGED

SIR,—Dr. Wilson's article of Sept. 4 is particularly valuable for its emphasis on training the bladder as one trains a disabled limb or defective eye or even the actions of speech.

Cystometry is still used far too little in both neurological and urological investigations. Some months ago I drew attention to the value of this procedure in the assessment of children with enuresis.[1] Doctors today are far too ready to send to the psychiatrist either the child or the adult who happens to be antisocial in that bladder control is defective. Let us see that we call on the psychiatrist as an aid in functional disorders and not merely to rid ourselves of the tedium and burden of full investigations on an organic level.

London, W.1. D. F. ELLISON NASH.

BOVINE PLASMA

SIR,—With reference to the articles on this subject which have appeared in your columns during the past two years,[2] we should like to inform you of the results obtained in our laboratory.

Denatured calf plasma (D.C.P.) prepared by us exactly as described by Massons (as well as a sample of D.C.P. prepared by Massons himself) has been found to possess strong anaphylactogenic properties. In experiments on guineapigs it was found that, while shock-provoking power is completely absent, the sensitising power is still present, although the lethal dose of fresh bovine plasma for guineapigs sensitised with D.C.P. is twice that necessary to shock the controls sensitised with fresh plasma. The interval between the two injections was 45 days. In practice this would preclude the use of a preparation of horse plasma but not of bovine plasma, since fresh bovine plasma is not commonly used.

Even so it is of interest to record the disagreement between our results and those obtained by earlier workers; this disparity would appear to be accounted for by the technique employed by these workers, which is obviously inadequate to demonstrate the sensitising and shocking properties of plasma. In fact the latent period increases with increase in the sensitising dose of antigen; and it is very long for doses greater than 0·1–0·2 ml. of serum or plasma.

E. CARLINFANTI
Director
M. PONTECORVO
Assistant
Naples. Istituto Sieroterapico Italiano.

1. *Practitioner*, 1947, **159**, 188.
2. Massons, J. M. *Lancet*, 1946, ii, 341. Melka, J., Rapant, V., Zapletal, B. *Ibid*, 1947, ii, 382. Boesen, C. E., Larsen, V., Nielsen, A. K. *Ibid*, 1948, i, 325. Barsoum, H. *Ibid*, p. 346. Annotation, *Ibid*, p. 332.

ACUTE BENIGN DRY PLEURISY

SIR,—In the interesting article by Dr. Gray and Dr. Carter (Aug. 14) I noticed that this condition was referred to as Bornholm disease. Actually, the condition was first described in Telemark, Norway, by Dr. A. Daa in 1872, and it was later called Bamble disease, as the first cases were reported from a district of that name. The same condition was observed in Iceland by Finsen in 1856 and 1863, but his findings were not published until 1874. In the U.S.A. the disease was observed and described by Dabney in 1888. Syvest's splendid treatise on this subject was published in 1933.

Porsgrunn, Norway. A. SCHRUMPF.

HANDLING OF FOOD

SIR,—The supply of pure food is, in theory, ensured by legislation; but failure to store and prepare it in cleanliness and freedom from contamination until it reaches the consumer is so common that one is tempted to suspect the absence of any legislation by which these measures may be enforced.

Similarly, the cleansing of cups, glasses, knives, forks, and other utensils used in the preparation and serving of food and drink is commonly carried out in so perfunctory and careless a manner that there is a real risk of infection. It is not that the local sanitary authorities are not empowered to use compulsion in these matters and in the maintenance of hygienic conditions in kitchens and larders where food is stored and handled; they are. Endeavours have been made to secure these ends, as Dr. F. A. Belam, medical officer of health for Guildford, has so aptly put it, "by persuasion," but people will always be found on whom persuasion has little effect.

It seems to me that the time has come for reviewing the whole of the legislation governing this subject and tightening it up. The duties of medical officers of health are so multifarious in these days that frequent inspections of premises may be difficult. A weak link in the chain from producer to consumer could easily be responsible for serious disease. Cases of food-poisoning are becoming far too frequent, largely because so many people now feed out in public restaurants who never did so before. Recent episodes which have occurred within my own experience will give point to my remarks:

A patient of mine went to her butcher's for the weekly meat ration. She described the shop as "full of bluebottles," which were flying about and settling on joints of meat in the window. While the butcher was conversing with another customer she noticed that his hand was slowly stroking a piece of meat. To her horror she saw that it was covered with maggots which the butcher was surreptitiously—as he thought—sweeping off with his hand.

A butcher, whom I knew to be suffering from a septic discharging sore on a finger, was handling meat with a bloodstained piece of rag round the finger. I asked him whether he thought it was a very good thing to do, not only for his own safety but for that of the meat. "Oh, the cooking will kill all the germs," he replied.

I saw a baker's roundsman taking loaves from his van and putting them in a basket for delivery to customers. He dropped one on the road, which was wet after a recent shower. He picked it up, looked at it, wiped it on the side of his trousers, and put it in the basket for delivery with the rest.

I was called to see a patient who had advanced carcinoma of the tongue and secondary involvement of glands in the neck which were on the point of breaking down. He had refused operation and hospital treatment. The stench was so horrible that I smelt it directly the front door was opened. The whole house reeked of it, and in his room, where the windows were shut, it was almost unendurable. He was also a chronic alcoholic—for which I did not blame him—and was in the habit of going out in the evening to two public-houses and returning home intoxicated after closing time. It was the practice at these public-houses to clean the tumblers by swishing them round in a receptacle of cold water under the counter and wiping them. They looked quite clean.

My wife and I went to a well-known London restaurant for luncheon at the most crowded time of the day. There were no tumblers on the table and I asked the waitress to bring some. She put them on the table dripping wet, and I noticed that the rim of mine was greasy and had traces

Digitized by Google

of lipstick. When I called her attention to it she wiped them hurriedly on what appeared to be a damp and dirty table napkin and replaced them on the table as "clean."

One has only to think of all the conditions in which infection is carried in the mouth—oral sepsis, diphtheria, syphilis, and the rest—and of common methods of cleansing drinking and eating utensils to realise the need for urgent reform. The answer appears to be threefold: legislation, education, and equipment. A study of the meticulously hygienic methods evolved and practised in the United States would be well worth while.

Brookwood, Surrey. H. M. STANLEY TURNER.

Public Health

NIGHTSHADE POISONING

Two outbreaks of nightshade poisoning have lately been observed in the south of England—one due to *Atropa belladonna* (deadly nightshade) and the other to *Solanum dulcamara* (woody nightshade).

DEADLY NIGHTSHADE

On the afternoon of Sept. 1 a party of children went blackberrying, at Milton, Portsmouth, on a plot of waste ground where, entwined among the stems of two large blackberry bushes, were several deadly nightshade plants, also bearing large black berries. The next day five of the children were admitted to hospital with acute belladonna poisoning.

The first three children to be admitted were two sisters and a brother, aged 7 and 8, who were said by their mother to have returned home at about 5 P.M. on the previous afternoon. Complaining of tiredness and thirst, they refused tea, but appeared normal; and two hours later, at 7 P.M., they went to bed and slept. At 9 P.M. they were awake, and in rambling speech complained of being unable to see. One child "kept falling about the room," and their mother thought that all three had a high temperature. On admission to hospital the next morning, all three were very restless, constantly executing purposeless movements, twisting about, grimacing, and plucking at the bedclothes. Two were talkative and obviously hallucinated, and their speech was a little slurred; the third, who lay with her head buried in the pillow fiercely resisting interference, seemed to have some photophobia. All three had hot dry skins and a pronounced malar flush; the lips were dry and fissured. The pupils were widely dilated and unresponsive to light; all tendon reflexes were brisk. The pulse-rate in each case was 120–130 per min.; the temperature was normal and the respiratory-rate was not increased. The highest blood-pressure was in the boy, in whom it was 138/80 mm. Hg.

Later the same morning a fourth child was admitted. After returning from the blackberrying expedition on the previous day he had had a large tea at 6 P.M.; at 9 P.M. he had gone to bed, apparently well. At 2.30 A.M. he was found struggling with his elder brother; he spoke incoherently, seemed not to recognise his parents, and kept picking imaginary objects off the bedclothes. At 4 A.M. he was given morphine by his doctor, and remained drowsy until admission at 1.30 P.M.

Soon after this, a fifth child, aged 6 years, was admitted. On his return from blackberrying he had had supper at 7.30 P.M. and gone to bed. During the night he was awake and twice vomited. At 6.30 A.M. both parents went out, leaving him in charge of an elder sister, who had summoned help at 12.30 P.M. because he was talking strangely.

Treatment.—On admission gastric lavage was carried out on all five children, first with plain water, then with potassium permanganate gr. 10 to the pint. This induced vomiting. Among the first three cases, over 30 berries were recovered from the boy's vomitus and nearly as many from that of each of his sisters. The berries in the gastric contents closely resembled raisins, but the seeds were smaller and darker than raisin "stones." No berries were recovered from the stomachs of the last two admissions. From rectal wash-outs no seeds or berries were recovered. Four hours later gastric lavage was repeated and in the first three cases several more berries were obtained. In each case a solution containing magnesium sulphate gr. 90 was introduced into the stomach.

Progress.—Late on the evening of Sept. 2 the children's condition was not appreciably changed; all were still extremely restless and hallucinated, with persistently high pulse-rates. All were incontinent; but there was no evidence of urinary retention. During the night they slept sporadically, and by 9.30 the next morning (Sept. 3) all except the boy in the first group were quieter and fairly coöperative, though suspicious and resentful of examination. They complained of great thirst, and two of them of severe frontal headache; malar flush was still pronounced, but the pupils were smaller and reacted slightly to light. The saline aperient was repeated; and that evening large numbers of seeds and berry skins were still being passed by each of the first three cases. Of these three, the boy is estimated to have eaten at least 40 berries and his two sisters 20–30 each. The physician in charge of these patients adds: "Why no berries or seeds should be recovered from the other children, whose symptoms were no less severe, is a mystery." The important features in these cases, he suggests, are as follows:

1. The long time between the ingestion of the berries and the appearance of symptoms.
2. The prominence of hallucination and the absence of fever or respiratory depression.
3. The significance of "raisins" in the vomit (unlike fresh deadly nightshade berries), which might not have been appreciated in the absence of a history that berries had been eaten.
4. The necessity in such cases as these of administering an emetic; many of the berries would have blocked the largest stomach-tube.

WOODY NIGHTSHADE

A girl, aged 9 years, was admitted to hospital at Canterbury on Aug. 13, with abdominal pain, thirst, vomiting, and distressed breathing. She had been in the habit of eating berries from hedges near her home, and had last done this 3 days before admission. The following day she had felt unwell but had improved. She had vomited "coffee-ground" material four times during the five hours before admission; there was no diarrhœa. She looked exhausted and anxious; her pulse-rate was 140 per min., and her skin was pale and dry. Her pupils were of normal size and reacted to light. Treatment included gastric lavage, soap-and-water enemas, nikethamide, and latterly oxygen; fluids were given by mouth and per rectum. After 24 hours her condition, which had improved somewhat, deteriorated again, with increasing weakness, cyanosis, and feeble respiration. She died on the morning of Sept. 15.

At necropsy the principal finding was acute inflammation of the mucosa of stomach and small intestine, decreasing in intensity towards the distal end. Analysis of the liver revealed the presence of solanine.

Notification of Infectious Diseases

ENGLAND AND WALES

Disease	Week ended Aug. 7	14	21	28
Cerebrospinal fever	40	38	26	29
Diphtheria	107	106	116	123
Dysentery	111	107	111	70
Encephalitis lethargica	...	...	3	2
Measles, excluding rubella	6879	5897	4611	3774
Ophthalmia neonatorum	44	75	59	55
Paratyphoid fever	47	19	20	17
Pneumonia, primary or influenzal	363	282	266	240
Polioencephalitis	5	2	6	7
Poliomyelitis	38	37	72	70
Puerperal pyrexia	135	88	106	100
Scarlet fever	848	774	736	812
Smallpox	...	...	...	...
Typhoid fever	10	8	8	12
Whooping-cough	3185	3458	3260	3162

Digitized by Google

Obituary

THOMAS GWYNNE MAITLAND

M.A., M.D., B.SC. EDIN., D.PHIL. MANC.

Dr. T. G. Maitland, who died on Aug. 10, was from 1926 until his retirement in 1946 medical superintendent of the Cunard White Star Line.

Born at Merthyr Tydfil in 1875 he was educated at University College School, London, and at the universities of Edinburgh, Manchester, and Paris. In 1907 he graduated in medicine at Edinburgh, and he was awarded distinction for his M.D. thesis the following year. He then took an honours course in philosophy at Manchester, proceeding to the D.PHIL. in 1911. After holding a resident appointment at the Brompton Hospital, he became demonstrator of physiology at Manchester, and later lecturer in the same subject at the universities of Wales, Birmingham, and Manchester. For a time, also, he was honorary physician at the Walsall and District Hospital. His literary interests led him to edit the *Manchester Medical Gazette* and to become co-editor of the *Midland Medical Review*. During the 1914–18 war he was director of the typhus colony at Skoplje in Serbia, and he was made an honorary lieut.-colonel in the Serbian Army.

In 1920 he joined the Cunard Company and for six years he acted as medical officer in one or other of the new ships which were laid down and commissioned to replace those lost in the war. They were years which saw a big development in winter cruising, and Maitland had to meet the new problems which arose in mercantile medicine as ships designed for the North Atlantic trips had to be adapted for long voyages in semitropical waters. In 1926, he succeeded Dr. David Morgan as Cunard medical superintendent, with the task of supervising the medical and nursing work of the ships, the medical aspects of living on board ship, and the equipment of ships' surgeries and dispensaries and hospital installations.

With the requisitioning of ships for transport and other war work in 1939, a host of new problems had to be met, and Maitland's help was sought far beyond the confines of his own organisation. Nothing in the medical aspect of life at sea was beyond the range of his interest; he carried out a good deal of research into seasickness, for example, and he took a large share in the establishment of the radiomedical service, whereby ships with no doctor aboard obtain medical advice by wireless. After he retired from the Cunard White Star Line, it was not long before he felt that he would like to go to sea again. He made a long voyage, as ship's doctor, to the Far East but found the heat too much for him. He came back knowing that the voyage had not been a success, and his friends realised that it had taken a great deal out of him.

"Maitland always said," writes R. C., "that he was primarily a philosopher; but he was a very human one, and his interest in workers on board ship and especially at the docks led him with quiet but terrier-like determination to insist that adequate first-aid centres and accident hospitals were established right in the heart of these dangerous occupations. The Merseyside and Birmingham Accident Centres owe much to his persistence. Perhaps more than any other man he improved immeasurably the status and quality of ship's doctoring. Working in the background, he brought his intelligence and keenness to the support of industrial medicine, for his interests went far beyond the sphere of his own job. He quietly encouraged young consultants to do a voyage across the Atlantic and back, knowing that on a long-term view it would benefit both them and the mercantile medical service. Often he would gather together a little group of doctors of diverse interests at a lunch party on one of his ships in dock. They were memorable affairs, and talk on all sorts of medical and other matters waxed fast and furious. In his later years at least he was a frail-looking man, with a limp from a painful arthritis and the disability also of a duodenal ulcer, but these things did not crush his spirit. Meeting him, you were aware at once that here was a remarkable personality, a man of quiet distinction and fineness of quality, a man moreover who delighted to pull your leg, who loved good talk and company, and who enjoyed both subtle wit and happy fun. With his death some of the warmth has gone out of life."

ANDREW RADBURNE FULLER

M.R.C.S., D.P.H.

Dr. A. R. Fuller, of Perranporth, Cornwall, who died on July 19 at the age of 55, was the elder son of Dr. Andrew Fuller, chief medical officer for England and Wales under the Local Government Board. He was educated at Leighton Park School and St. Mary's Hospital, at both of which he won open scholarships. In September, 1914, he went to France with the Red Cross as a medical orderly, returning in 1915 to finish his medical course. Immediately after qualifying in 1916, he was commissioned in the R.A.M.C. and posted as a battalion medical officer to a division in the Battle of the Somme. Early in 1917 he was sent home to spend many weary months in hospital and was invalided out in 1920. In the same year he took his D.P.H., and he joined his father in practice at Perranporth in 1921 where he remained until his death.

"Fuller," a colleague writes, "will long be remembered by all in Perranporth and the surrounding district for his medical ability and devotion to his work, which he combined with a sincere and unselfish love of his fellow men. He upheld the finest traditions of the profession. A keen athlete, he was a first-class cricketer and tennis player, holding the Cornish singles championship for three successive years and also playing first couple for the county."

Dr. Fuller married in 1925 Elizabeth Mary, younger daughter of Dr. Peter Ingram, of London, and he leaves his wife with a son and a daughter. A twin son died in 1943.

Appointments

DICKS, H. V., M.A., M.D. Camb., F.R.C.P.: senior psychiatrist, Tavistock Clinic, London.
GOODDY, W. W., M.D. Lond., M.R.C.P.: registrar, National Hospital for Nervous Diseases, London.
GRACIE, A. P., M.B. Edin., F.R.C.S.E.: accident officer, Salford Royal Hospital.
ROSS, M. S., M.R.C.S.: clinical pathologist, Queen Mary's Hospital for the East End, London.
WILDMAN, J. H., M.R.C.S., D.P.H.: M.O.H., East Herts combined sanitary district.

Colonial Service:

AZZOPARDI, E., M.D.: M.O., Federation of Malaya.
BARTLEY, A. H., M.R.C.S.: M.O., British Honduras.
CHELMICKI, B. J., M.B.: M.O., Gold Coast.
CLUNIE, THOMAS, M.B. Aberd., D.T.M.: senior M.O., Fiji.
CRISP, THOMAS, M.R.C.S.: M.O., Uganda.
HANSEN, A. G. P.: M.O., Tanganyika.
MAXWELL, R. W. D., M.B.: senior M.O., Fiji.
PHILLIPS, B. L. C., M.R.C.S.: M.O., Hong Kong.
RAPER, A. B., M.D. Lond., B.SC. Leeds, M.R.C.P.: senior pathologist, Uganda.
STEENSON, K. R., M.B.: senior M.O., Fiji.
WASE-BAILEY, B. N. V., M.D. Edin., D.T.M. & H.: asst. director of medical services, Sierra Leone.

Births, Marriages, and Deaths

BIRTHS

CUTTS.—On Sept. 1, in London, the wife of Dr. Geoffrey Cutts—a daughter.
FOX.—On Aug. 22, in London, the wife of Dr. J. P. Fox—a son.
ROCHE.—On Aug. 29, at Leeds, the wife of Dr. J. Roche—a son.
SHILLINGFORD.—On Aug. 31, in London, the wife of Dr. J. P. Shillingford—a son.

MARRIAGES

SEARS—CONN.—On Sept. 4, at St. Andrews, Harold Trevor Newton Sears, M.R.C.P., to Janet Sorley Conn, M.B.

DEATHS

FRENCH.—On Aug. 29, at Nairobi, Stanley Gay French, M.B. Lond., F.R.C.S., surgeon lieut.-commander, R.N., aged 40.
MARRIOTT.—On Aug. 30, Francis Keene Marriott, M.C., M.R.C.S.
MURRAY.—On Aug. 9, at Dornoch, Sutherland, David Alexander Murray, M.B. Edin., aged 50.
PATERSON.—On Aug. 28, in London, Arthur Robert Paterson, M.D. Brux., major I.M.S. retd., aged 88.
RASHLEIGH.—On Aug. 29, at St. Peter's-in-Thanet, Hugh George Rashleigh, M.R.C.S., aged 72.
WHEATON.—On Sept. 5, Samuel Walton Wheaton, M.D. Lond., F.R.C.P., D.P.H., aged 86.
WIGMORE.—On Aug. 29, at Minehead, A. J. O. Wigmore, M.B. Brist., squadron-leader, R.A.F. retd., aged 63.

Digitized by Google

Notes and News

CASE OF OSCAR WILDE

FIFTY years ago Oscar Wilde was not mentioned in polite society. The account of his trials, now published in full[1] under the editorship of Mr. Montgomery Hyde, might then have been brought to the notice of a metropolitan police magistrate for possible suppression and punishment as an obscene libel. Times have changed.

In 1885, during the passage of the Criminal Law Amendment Bill which dealt with the protection of women and girls, Labouchere secured the insertion of a clause (afterwards section 11) creating the offence of indecency between male persons in public or private. Under this section Wilde was eventually tried ten years later. Son of the well-known Irish ophthalmic and aural surgeon, Sir William Wilde, he distinguished himself in classics at Trinity College, Dublin, and, going on to Oxford, obtained two first-classes and the Newdigate prize for English poetry. He married the daughter of an English Q.C. and had two children. If the extravagances of his cult of æsthetic philosophy were caricatured in W. S. Gilbert's *Patience*, his poems and fiction were not to be despised, and his plays were brilliant.

At the age of 38 he made the acquaintance of Lord Alfred Douglas, then 22 years old, the third son of the eccentric Marquis of Queensberry. Father and son hated one another. Violent and vindictive as the Marquis was, he had some justification for objecting to Wilde's intimacy with his son. After threats and abuse, he went to Wilde's club and left for him with the hall-porter a card with the curiously mis-spelt inscription: "For Oscar Wilde posing as somdomite." Largely influenced by Lord Alfred, who saw a chance to strike at his father, Wilde prosecuted the Marquis for criminal libel. Sir Edward Clarke, first obtaining from Wilde the most solemn assurance that there was not, and never had been, any foundation for the allegations against him, undertook the prosecution. Carson was briefed for the defence; the Marquis filed particulars in justification and pleaded that publication had been for the public benefit. Wilde in the witness-box held his own for a time against Carson's cross-examination, displaying the sparkling, if flippant, wit which distinguished his two plays (*An Ideal Husband* and *The Importance of Being Earnest*) then drawing big audiences. But a change came when Carson put to him the names of a series of youths of humble station to whom (as Wilde admitted) he had given dinners, money, and valuable presents. If these young men were called for the defence their evidence might be discounted as that of self-confessed accomplices and, in some cases, blackmailers; but Clarke, highly competent and experienced, advised the breaking off of the prosecution. The Marquis, after all, had accused the prosecutor of "posing," not of actual commission of the crime. A verdict of "Not guilty" was entered and the particulars of justification were thus accepted. Carson's clients sent to the director of public prosecutions a copy of their witnesses' statements; a warrant for Wilde's arrest was applied for; he had time to fly the country, but he did not go. Clarke, maintaining at all times the highest standards of the bar, wrote an offer to defend Wilde without fee in the proceedings which followed.

The arrested man needed indeed all the help he could muster. The press was hostile; his books were struck out of publishers' lists; one of his plays was taken off forthwith, the other a few weeks later; money was short. Charles Gill prosecuted him at the Old Bailey, Carson refusing to have anything more to do with the case. The jury disagreed after five days and a re-trial was ordered. This time the solicitor-general, Sir Frank Lockwood, was for the prosecution; no stone was left unturned. Wilde was convicted and Mr. Justice Wills imposed the maximum sentence of two years' hard labour.

The *Ballad of Reading Gaol* and the biographical memoirs of Lord Alfred Douglas and others kept alive, not without recrimination, various personal questions which matter little now. Had the trials taken place today, the court might have been invited to consider Wilde's mental state. Mr. Montgomery Hyde, in his careful editing of the proceedings, adds one appendix on "The Problem of Wilde's Inversion" and another on "The Prevalence of Male Homosexuality in England." He recalls that, during a debate in the House of Lords in July, 1937, Lord Dawson of Penn observed that homosexuality was now regarded as a pathological state and might even some day be deemed an "insufficiency disease," or at any rate as much disease as crime. It may, however, take another fifty years to convince the judges and the British public that these cases are other than—to quote Lord Atkin's opinion delivered in the same debate—"the result of wicked impulses which, like other wicked impulses, are capable of being controlled and can be checked by advice and by resolution."

1. *The Trials of Oscar Wilde.* Edited by H. Montgomery Hyde, with a foreword by Sir Travers Humphreys: Notable British Trials Series. London: Wm. Hodge. Pp. 384. 15*s*.

OPTION UNDER SUPERANNUATION REGULATIONS

IN a circular letter (E.C.L.80) the Ministry of Health points out that those practitioners who wish to contract out of the National Health Service superannuation scheme must give notice by Oct. 4. This option, as was explained in our issue of July 3 (p. 39), is open only to those who are covered by insurance policies.

OUTPATIENT FACILITIES FOR PSYCHIATRIC CASES

THE National Association for Mental Health has just published a 43-page directory of child-guidance clinics and outpatient clinics for adult patients. Addresses are given in all counties in England and Wales and Northern Ireland: Scottish inquirers are referred to the Scottish Association for Mental Hygiene. General practitioners, almoners, and social workers will find this list useful. Copies may be obtained (1*s*. each or 11*s*. per doz.) from the N.A.M.H., 39, Queen Anne Street, London, W.1.

Edinburgh Post-Graduate Board For Medicine

On Thursday, Sept. 16, at 4.30 P.M., in the anatomy lecture theatre of the university, Prof. J. C. Brash will speak on Modern Trends in Anatomy.

Institute of Laryngology and Otology

On Tuesday, Sept. 14 at 5.15 P.M., at the institute, 330, Gray's Inn Road, London, W.C.1, Dr. A. C. Roxburgh will speak on Dermatology as it concerns the Ear, Nose, and Throat.

Institute of Psychiatry

Lecture and demonstration courses for postgraduate students in psychiatry will be held at the institute during the coming session. Further particulars may be had from the secretary of the institute, Maudsley Hospital, Denmark Hill, London, S.E.5.

Royal Free Hospital

On Friday, Oct. 1, at 3 P.M., Mr. L. E. C. Norbury will deliver the inaugural address of the school of medicine in the Beveridge Hall, Senate House, University of London, Malet Street, W.C.1. He is to speak on the Importance of Team Work with special reference to Hospital Life.

British Tuberculosis Association

At a meeting of the association to be held at 26, Portland Place, London, W.1, on Friday, Sept. 17, at 3.15 P.M. Dr. R. D. Lawrence and Dr. I. M. Hall will speak on Tuberculosis and Diabetes, and Dr. L. E. Houghton on Collapse Therapy and the Bronchus.

International Congress on Industrial Medicine

Members of this congress, which will open at the Central Hall, Westminster, on Monday, Sept. 13, at 11.30 A.M., may register on Sunday, Sept. 12, from 10 A.M. to 5 P.M., at Church House, Great Smith Street, S.W.1, and on Sept. 13, 14, and 15, at Caxton Hall, Westminster, from 9 to 10 A.M. and from 12.15 to 2.30 P.M. During the congress the secretary, Dr. H. J. Davies, may be addressed at room 16, at Caxton Hall.

AIR AMBULANCES.—Morton Air Services Ltd., who operate a world-wide service of air ambulances from Croydon Airport, inform us that their additional address at Liverpool, given in their advertisement of Sept. 4, has been cancelled.

CORRIGENDA.—The opening address at the *International Congress on Population and World Resources* was given by Lord Horder. Sir John Boyd Orr opened the discussion at the first session.

In the directions for the use of '*Clinitest*' (Sept. 4, p. 399) five drops of urine plus *ten* drops of water should be placed in a test-tube.

Digitized by Google

SEPT. 18, 1948 PAGES 441 TO 480

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6525 LONDON: SATURDAY, SEPTEMBER 18, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Clinical Research in the Education of the Specialist
Prof. W. M. ARNOTT, F.R.C.P.E. 441

Streptomycin in Non-tuberculous Infections
Prof. CLIFFORD WILSON, M.R.C.P. 445

Streptomycin Treatment of Meningitis Due to Gram-negative Saprophytes
WALPOLE LEWIN, F.R.C.S.
R. L. VOLLUM, D.PHIL. 446

Streptomycin in Pulmonary Tuberculosis
R. Y. KEERS, M.R.C.P.E. 449

The Eosinophil Cell
FREDERIC DURAN-JORDA, M.D. 451

Meningo-encephalitis in Man Due to the Louping-ill Virus
GEORGE DAVISON, M.R.C.P.
CHARLES NEUBAUER, M.D.
with serological report by
E. WESTON HURST, F.R.C.P. 453

Leontiasis Ossium
C. B. WAY, M.B. 457

SPECIAL ARTICLES

The Morals of Employment
T. A. LLOYD DAVIES, M.R.C.P. 465

Proprietary Medicines under the National Health Service Act
E. W. GODDING 465

International Orthopædic Congress in Quebec 467

Radioactive Isotopes for Clinical Research 469

PUBLIC HEALTH

Hygiene in Palestine
ERIC HARDY, F.Z.S. 470

Two Outbreaks of Typhoid Fever 471

Paratyphoid at a Girls' Camp 471

LEADING ARTICLES

DIETARY FAT 459

SUPPLIES OF RADIOACTIVE ISOTOPES 460

HEALTH CARE 461

ANNOTATIONS

The Industrial Congress Opens .. 462

A Piperazine Anthelmintic 462

Streptomycin in Non-tuberculous Infections 462

Posture in Anæsthesia 462

Hospital Building 463

Student Nurses' Salaries 463

Legitimacy and Artificial Insemination 463

The Health Centre 464

Index to THE LANCET 461

LETTERS TO THE EDITOR

The Agricultural Worker (Dr. Robert Wigglesworth) 473

Salaries in Government Service .. 473

Student Selection (Dr. E. Geiringer) 473

Exsanguino-transfusion in Acute Leukæmia (Dr. W. d'A. Maycock) 474

Shortage of Blood for Transfusion (Dr. A. Piney) 474

Cause of Primary Hepatic Carcinoma (Dr. J. N. P. Davies) .. 474

M.R.C.P. Examination 475

Letter to a Nephew (Dr. Thomas Nelson) 476

Importance of Fat in the Diet (Mr. A. R. P. Walker, PH.D.) .. 476

Life and Death in a Concentration Camp (Dr. Juraj Oravec) 477

Homologous Serum Hepatitis (Dr. F. O. MacCallum; Dr. D. J. Bauer) 477

Man into Wolf (Dr. J. D. Molina) 477

Postcricoid Pharyngo-œsophageal Perforation Due to Endoscopy (Dr. Karsten Kettel) 478

Accidental Intra-arterial Injection of Drugs (Mr. G. C. E. Simpson, F.R.C.S.) 478

REVIEWS OF BOOKS

Acute Intestinal Obstruction. Rodney Smith, F.R.C.S. 458

Eat and be Healthy. Lucius Nicholls, M.D. 458

Principles of Occupational Therapy. Helen S. Willard, B.A., Clare S. Spackman, B.S. 458

Juvenile Delinquency in an English Middletown. Hermann Mannheim 458

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 472

OBITUARY

Samuel Walton Wheaton 478

The late Professor Jamieson 479

NOTES AND NEWS

Prof. Jörgen Schaumann 480

Reproduction Explained to Children 480

University of London 480

University of Sheffield 480

University of Glasgow 480

University of Aberdeen 480

Royal College of Physicians of London 480

Royal Faculty of Physicians and Surgeons of Glasgow 480

King's College Hospital 480

Westminster Hospital 480

Middlesex County Medical Society 480

International Scientific Film Congress 480

West London Medico-Chirurgical Society 480

British Hospitals Contributory Schemes Association 480

Chadwick Lectures 480

Diary of the Week 480

Appointments 479

Births, Marriages, and Deaths ... 479

Founded 1892 Assets exceed £120,000

The MEDICAL PROTECTION SOCIETY Limited

President: SIR ERNEST ROCK CARLING, F.R.C.P., F.R.C.S., F.F.R.

Established for the protection of the professional interests of medical and dental practitioners. Members receive advice and assistance in all matters affecting the practice of their profession and are afforded COMPLETE INDEMNITY against costs and damages in cases undertaken on their behalf.

Entrance Fee 10/-

Annual Subscription £1 Membership Exceeds 23,000

No entrance fee to those joining within 12 months of registration

An additional subscription will secure indemnity in respect of practice overseas

Full particulars and application form from—

The Secretary, VICTORY HOUSE, LEICESTER SQUARE, W.C.2. GERrard 4553 & 4814

Digitized by Google

OXFORD MEDICAL PUBLICATIONS

HEPARIN

By J. ERIK JORPES, *M.D.*
Reader in Biochemistry, Karolinska Institutet, Stockholm
With a Foreword by J. R. LEARMONTH, *C.B.E., F.R.S., Ch.M., F.R.C.S.*

'An authoritative and timely monograph.'—*British Medical Journal.*

SECOND EDITION 260 *pages* 24 *illustrations* (2 *in colour*) 18*s. net*

OXYGEN AND CARBON DIOXIDE THERAPY

By ARGYLL CAMPBELL, *M.D., D.Sc.*
Member of the Research Staff, National Institute for Medical Research
and
E. P. POULTON, *M.A., D.M., F.R.C.P.*
Physician to Guy's Hospital
With a Foreword by SIR LEONARD HILL, *F.R.S.*

'The only really complete book devoted to this subject.'—*Post Graduate Medical Journal.*

216 *pages* 56 *illustrations* 15*s. net*

BREAST FEEDING

By F. CHARLOTTE NAISH, *B.A., M.D.*
Honorary Medical Officer to Heworth Moor Hospital
(Sir Charles Hastings Clinical Essay Prize, 1947)
With a Foreword by ALAN MONCRIEFF, *M.D., F.R.C.P.*

'All concerned with the establishment and maintenance of natural feeding will profit from reading her book.'—*Lancet.*

164 *pages* 20 *illustrations* 10 *tables* 10*s. 6d. net*

PSYCHOTHERAPY: ITS USES AND LIMITATIONS

By D. R. ALLISON, *M.D., M.R.C.P.*
Honorary Physician to Stockport Infirmary
and
R. G. GORDON, *M.D., D.Sc., F.R.C.P.*
Consulting Neurologist to Stoke Park Colony

'Common sense approach and reasoned tone . . . amply succeeds in its aim.'—*Mental Health.*

168 *pages* 8*s. 6d. net*

THE BACKGROUND OF THERAPEUTICS

By J. HAROLD BURN, *M.D., F.R.S.*
Professor of Pharmacology in the University of Oxford

'Few recent books will give so much pleasure to the thinking doctor.'—*Lancet.*

376 *pages* 59 *illustrations* 26 *tables* 22*s. 6d. net*

THE PARATHYROID GLANDS AND SKELETON IN RENAL DISEASE

By J. R. GILMOUR, *M.R.C.P.*
Junior Assistant Director, Bernhard Baron Institute of Pathology, London Hospital

'A major contribution to the pathology of the parathyroids and a further step in the elucidation of the complex mechanism controlling calcium and phosphorus metabolism.'
—*Journal of Pathology and Bacteriology.*

172 *pages* 26 *illustrations* 18*s. net*

OXFORD UNIVERSITY PRESS

Digitized by Google

HISTORICAL BUILDING
DES MOINES, IOWA

CLINICAL RESEARCH IN THE EDUCATION OF THE SPECIALIST *

W. MELVILLE ARNOTT
T.D., M.D., B.Sc. Edin., F.R.C.P.E., M.R.C.P.
WILLIAM WITHERING PROFESSOR OF MEDICINE IN THE UNIVERSITY OF BIRMINGHAM

ONE hears much these days about research; indeed in relation to clinical medicine it almost threatens to become a bone of contention. Clearly, there is a wide difference in the interpretation of the term. To some research seems to be synonymous with the paraphernalia of the laboratory and with the esoteric techniques of modern chemistry and physics; to others it is the production of papers; and to all too few it is essentially an intellectual approach.

One of the most attractive and stimulating articles of the appointment I hold is that which charges me with the personal conduct, organisation, and direction of research. The endeavour to discharge this obligation necessitates much thought and experiment directed to ascertaining the optimum methods of design and prosecution of investigation. These are pressing matters which face many; feasible solutions are vital to the success not only of the many whole-time university clinical departments that are being established but also to the whole future of clinical practice.

In the various recent memoranda on specialist training that have come from the Royal Colleges there has been uniform insistence on a period of a year or so of the five years of apprenticeship being spent in work in the so-called basic sciences. There is a tendency to imply that this year should be non-clinical and should be taken in the departments of anatomy, physiology, chemistry, &c. Though these departments provide admirable training, it should be possible to provide equally good and perhaps even better opportunity for training in the scientific method in clinical departments. Indeed the distinction will, I feel sure, become increasingly nebulous as the preclinical and clinical departments of our medical schools find increasing community of effort in teaching, research, and clinical practice.

There has unfortunately been in the past a measure of dissociation between those in laboratory work and those in clinical practice, which has been harmful to both groups and has been due to faults on both sides. The non-clinical scientist has sometimes believed that his clinical colleague is not only incapable of but even contemptuous of the scientific method, while the clinician in his turn has sometimes felt that the "lab man" is blind to the problems of clinical practice and insensitive to the humanitarian appeal. Such schisms are closing, and medicine, in Britain at least, is entering an era of integration and coöperation which will favour new discovery and rational practice.

STATISTICS

What contribution should the study of research methods, or the actual prosecution of research, make to the training of the specialist in medicine? Obviously in the allotted time it can give comparatively little by way of detailed technical knowledge. Its main purpose must be to develop the habit of mind which is attuned to the challenge of the unknown, is continually seeking to improve the precision of observation, and in the exercise of diagnosis or the assessment of therapeutic effort places reliance on phenomena in inverse proportion to their inherent variability. Whatever else is learnt in medical training, a sound appreciation of the value of the quantitative approach is essential. The evolution of every branch of science has been through the descriptive stage to the maturity of the increasingly precise application of the quantitative language of mathematics. Biology, and particularly clinical biology, has presented peculiar resistance to this evolutionary process, but this is being steadily overcome. One has only to consider the development of clinical chemistry and the recent rapid development of quantitative methods in the clinical physiology of the cardiovascular system to realise the increasing application of physical and chemical techniques to human function and dysfunction.

The most important forward influence is the steady penetration into clinical practice of the principles of statistical thought. The intelligent practice of medicine, and especially investigative medicine, is inescapably bound up with degrees of probability and improbability based on accumulations of numerical data. It is not so long since the techniques of statistical analysis were reserved for the vital statistics of large populations and were the exclusive perquisites of the Registrar-General, the medical officer of health, and the insurance actuary. However, the brilliant researches of R. A. Fisher and his colleagues have developed the mathematical treatment of small groups of observations, and the methods evolved at the Agricultural Research Station at Rothamsted are eminently suited to the numerical observations of the ward and of general practice. Most of the reputable medical journals now require numerical data submitted to them to show evidence of quantitative assessment of degrees of significance or of correlation, and an increasing number of valuable contributions have only been possible by the application of the more advanced methods of the analysis of variance, &c. Unfortunately it is still possbile to cull from current medical literature numerous examples of false conclusions based on the uncritical assembly of quantitative observations.

The education of the doctor, be he a specialist in clinical practice or a specialist in clinical research, requires not so much the acquisition of mathematical techniques as the development of a sense of the variability of biological measurement and of the existence of methods of measuring, controlling, and explaining this variability. The modern medical teaching and research organisation has its statistical department to which the research-worker can turn not only for guidance in the assessment of results already obtained but also for the design of experiment to ensure that the maximum of information is obtained with the minimum of effort. I believe that much of the aversion to the use of quantitative methods in clinical research is due not so much to any inherent difficulty in grasping the common-sense principles as to the drudgery of the arithmetic involved. For that reason I encourage all members of my department to make the fullest possible use of the slide-rule, the Otis King Calculator, the electric calculating machine and books of mathematical tables. Emphasis should also be placed on the amount of information that can be got from the simple graph. Graphic records in clinical work tend to be restricted to records of temperature, and pulse and respiration rates, while much valuable information is missed and many suggestive correlations pass unnoticed because nobody has bothered to plot other observations. I heard of a teaching hospital in which the only height yard stick was in the nurses' home, and nobody had even heard of a patient's height being recorded, with the result that it is impossible to relate the wealth of numerical data contained in its case-records to the norms of height, weight, and age.

The habit of quantitative and statistical thought is not only essential to research but also has a profound influence on the quality of observation without which good practice is impossible. A person so trained is continually questioning the accuracy of the data on which he makes his diagnosis or modifies his treatment.

* From an address delivered to the Harveian Society of London on May 19.

Digitized by Google

He knows that the emphasis he can place on, say, his clinical location of the apex-beat as an index of heart size is strictly related to the accuracy of this method as checked by radiological or pathological examination; that the significance of pain in the right shoulder as evidence of gall-bladder disease depends on how often it is present in proven cases of disease of that organ and how often without such disease; and that the accuracy of the diagnosis of tuberculosis is much impaired if the tubercle bacillus is not isolated.

Quantitative and critical thought confers some immunity to the cardinal sin of certitude, the commission of which betrays a flaw as fatal in the daily practice of the physician as in that of the laboratory worker. Respect for authority in science is based not on the ex-cathedra pronouncement but on the production of sound evidence which stands the test of significant correlation with observation. Clinical practice divorced from scientific discipline undoubtedly leads, or rather has led, to an atmosphere of authoritarianism in which the neophyte does not appreciate the difference between dogma and deduction, comes to have an undue veneration for the logos, and is apt to be blinded to the existence of gaping cracks in the structure of knowledge. Such a dangerous and prematurely senile attitude of mind will not develop in an organisation dominated by a spirit of inquiry in which patients are diagnosed in the light of the most accurate observations, both historical and physical, that human ingenuity can devise and are treated by the method which seems most rational, all with the keenest appreciation of the fallibility and imperfections of these procedures and with the dominant ambition to acquire new knowledge which will lead to better methods.

USE OF LITERATURE

An important part of training in scientific method consists of the proper use of literature. It is fatally easy for the medical specialist to fall into the habit of reading only the journals dealing with his particular branch. Not only must the trainee learn the use of the *Cumulative Index Medicus* and the pitfalls of being content with second-hand cited references, but also he must have ready access to those journals which report applications of the scientific method to clinical problems. Among this group, mention must be made of *Clinical Science* and the *Journal of Clinical Investigation*. The *Journal of Physiology*, though only in minor degree clinical, provides particularly good examples of the proper conduct of biological investigation. Ready access to complete sets of these journals is essential. *Nature* and *Science* provide breadth of outlook and are a fruitful source of new methods. From time to time discovery and technical advance in one department of science may provide the clue which will overcome an impasse in an investigation in a totally different field. Study of good scientific literature develops an appreciation of the importance of the proper reporting of observations and of the relatively ephemeral value of hypothesis and speculation. A large proportion of the interpretation and conjecture in scientific reports is, of necessity, incomplete or even erroneous, but data, especially quantitative data, adequately detailed with sufficient account of the methods to enable reproduction by others, is of enduring value and may provide an indispensable link in a chain of evidence which leads subsequent investigators to some important advance. Though it is given to few to make major forward steps, it should be within the power of many to contribute an accurately fashioned piece to the mosaic of knowledge.

DISCUSSIONS

The colloquium or seminar is a valuable feature of the clinical unit. It provides an opportunity for the trainee specialist to give an account of the progress of his research and to have his particular problem discussed. It should be the accepted thing that, when a research comes to an apparent impasse—and that, in my limited experience, is frequent—because of either technical difficulties or incomprehensible results, it should be put on the agenda for the next seminar. This not only provides an opportunity for others to share the mental exercise of the problem but also is surprisingly fruitful of solution. Such meetings are all the more valuable if, as in the case of my own department, they are regularly attended not only by clinical colleagues but also by physiologists, pathologists, pharmacologists, and statisticians. Such meetings should be quite distinct from staff clinical meetings, in which the emphasis is more on the study of the diagnosis and management of individual cases. In addition, directors of research should make a point of introducing, as often as possible, their junior associates to the scientific proceedings of such societies as the Medical Research Society, the Physiological Society, and the Pathological Society. Those whose investigative efforts meet with success will become eligible for membership of these societies.

TYPES OF RESEARCH

One comes now to an important aspect of the integration of research and specialist training—i.e., a review of the types of investigation. Such is necessary for one to be in a position to give counsel to the novice. Sometimes, of course, little advice is needed, in that the beginner comes with a clearly defined and limited problem which is well within the capabilities of the individual, the technical resources of the department, the supply of suitable cases, and the time available. Such a happy project is, however, extremely rare. When it presents, the originator should be the object of particularly close supervision, because, if to his prescience be added diligence and adaptability, he is likely to be worthy of rapid advancement in investigative medicine.

Apart from obligatory elementary training in research methods which may become an essential part of specialist training, the reasons which impel young men to devote time to investigation are often obscure. Some may merely want to produce a thesis acceptable for a higher degree; others may be profoundly dissatisfied with the glaring imperfections, obvious inconsistencies, and scarcely warrantable assumptions which characterise the established body of knowledge of some physiological phenomenon or disease process; others may be so constituted as to derive substantial mental and emotional satisfaction from the systematic approach to a problem. A few obviously have uppermost in their minds the desire to find out whether they are capable of original research, and if so whether a career devoted exclusively to research work or the combination of routine specialist practice with a research problem will provide the happiest outlet for their ambitions and abilities. It is important for those charged with the heavy responsibility of selecting candidates for the range of activities which lie between, on the one hand, a short training in research principles and methods as a part of specialist training, and, on the other hand, a career devoted to whole-time research to realise that "job selection" is as yet only at best approximate, and that the acid test is close observation during a trial period. Some types are, almost from the outset, clearly unsuited for anything more than elementary instruction in scientific methods as applied to clinical problems. Such persons are unusually dependent on guidance, both in their everyday clinical work and in the laboratory; they attach great emphasis to the opinions of seniors and have an uncritical regard for accepted hypotheses and dogma and an aversion to resolving problems to first principles. They may be likened to the navigator who is seized with panic when he finds himself in an unusual situation

Digitized by Google

deprived of one or more of his customary guides. Such a quality of mind is compatible with an extensive stock of theoretical knowledge and even with the capacity to teach with clarity and persuasiveness. In my opinion, however, such men are entirely unsuitable for research and for senior medical educational responsibility, because a very important function of university education is to teach what is known in the light of what is not known and to foster the attitude which regards the knowledge of today as a base from which to evolve the knowledge of tomorrow.

An elegant type of research is that which begins with an assembly of the available knowledge of some particular phenomenon and the erection on this basis of a hypothesis which seems to fit the data. This hypothesis is then used to predict the results of one or more series of experiments. These experiments having been performed, the degree of correlation between the predicted and observed is a measure of the validity of the hypothesis. More often than not in clinical science this technique gives a somewhat imperfect correlation indicating that some substantial variable has not been appreciated, or, as one statistical technique expresses it, the "residual variance" is of considerable magnitude. Two illustrations will illuminate this approach:

Goldblatt, from a wide range of unconnected clinical, pathological, and experimental data, formed the hypothesis that permanent reduction of renal blood-flow in mammals produced systemic hypertension. He tested this concept by graduated reduction of the lumen of the renal artery in dogs, with a relatively complete vindication of the validity of the hypothesis.

Some months ago in our own laboratory a research reached a point at which it became necessary to know with as high a degree of certainty as possible whether the air inspired with a deep breath was accommodated by an increased expansion of the alveoli in use during quiet breathing, or whether additional "reserve" alveoli became ventilated. With a knowledge of the volumes of the residual air, alveolar air composition, &c., and by the use of known degrees of admixture with an inert gas it was possible to predict the quantitative changes in alveolar air which could be expected on the basis of each of the conflicting hypotheses. Experimental observation furnished a very close correlation with the result predicted on the basis of the large breath being accommodated by distension of the same alveoli used in quiet breathing.

TRAINING OF RESEARCH-WORKERS

The beginner in research should not be allowed to embark on a project without preparing an outline of the hypothesis to be tested and of the possible answers which the experimental approach may yield. Often enough this preliminary theoretical approach will reveal that the design of experiment is fundamentally incapable of yielding the desired information, a discovery which is better made before time and effort are wasted. Though it may be clear from the outset that a certain minimum of experiments will be necessary to establish a significant answer, that should not deter the worker from the analysis of the results at short intervals. There is no more intellectually satisfying experience than to watch the degree of significance steadily increase with replication, and on the other hand there is no more mortifying trial than to discover after weeks or months of labour that the effort expended is largely in vain because some unpredicted factor or frank error has marred the results. The novice should be taught that it is when the results of his experiments seem most mysterious and inexplicable that he is most likely to make a new and exciting discovery. In research as in other spheres of endeavour it is when things go wrong, and doubt and difficulty beset, that ingenuity, morale, and stamina can best be assessed.

Often enough the beginner essays a research project far too broad and general in scope to allow of any real progress within a reasonable time; or necessitating such a range of technical processes as to imply an attack by a carefully selected team of experimental investigators. Without experienced direction the result is inevitable disillusionment and frustration, with the acquisition of a sadder and not necessarily wiser frame of mind, all too often tinged with cynicism and revulsion to investigative activity. The approach to a specific research project is along exactly the same lines as the conduct of a military operation—i.e., by the exercise of the scientific method. The problem to be solved is equivalent to the objective whose capture is desired. A critical study must be made of the available information—i.e., in the words of a famous manual of military tactics, "Time spent on reconnaissance is rarely wasted." A careful assessment must be made of the available resources in terms of apparatus, clinical material, and, above all, of the time required to acquire the necessary skills and to perform the experiments. Finally, a very generous time margin must be allowed for unforeseen delays due to technical difficulties, lack of suitable cases, and, to continue the military analogy, for unexpected resistance and difficulty in the reduction and consolidation of intermediate objectives. A full appreciation of the problem both in its abstract and concrete details will often reveal to the beginner the impracticable nature of his scheme; he will realise that he was proposing to engage on a corps front with battalion strength.

It is true that the measurement of cardiac output by the application of Fick's principle and the obtaining of samples of mixed venous blood from the right heart constitutes a valuable procedure, but the actual insertion of the cardiac catheter, in itself not very difficult, is only a dramatic incident in a broad background of skilled collection and gas analysis of samples of blood and respired air. The beginner will probably take much longer to acquire the necessary skill in handling the Van Slyke manometric apparatus than in learning to insert the catheter. If one adds to that the simultaneous recording of right auricular pressure by a Hamilton or Warburg manometer, the whole process becomes a matter for a highly trained team at least one member of which must be exclusively engaged in this work.

The use of radioactive isotopes in clinical research opens up glittering vistas of conquest of knowledge, but while deceptively simple in theory these techniques are complex and costly in application and are beyond the scope of any but the specially trained and experienced investigator.

It is sometimes necessary to disabuse the beginner of the notion that for him clinical research can be done by merely arranging for a series of tests to be performed by the biochemist, the clinical pathologist, or any or all of the various special departments found in the large modern hospital. Though the experienced clinician trained in research method, working in partnership with the biochemist, clinical pathologist, radiologist, &c., can achieve results of the highest order, "request reform research" methods in the hands of the inexperienced can become rich mines of misinformation and often prove an intolerable imposition on the various special departments.

In brief, it is one of the most important duties of the research director to guide his charges to a limited problem which is well within their scope and to make it perfectly clear to them that they must be prepared to carry out the technical details themselves at least as well as any technician. Only thus can they appreciate the variability of the measurements, and in actually doing the work themselves they are much more likely to see new and fruitful avenues of approach.

I know of a famous American laboratory where the research-workers have the minimum of technical assistance but adequate accommodation and excellent workshop facilities. This compulsion to find out and "do" for themselves provides ideal training. I look back with appreciation to the time when for months on end my colleague and I had to measure

Digitized by Google

the food and drink, and collect, measure, and analyse the urine, of our group of rabbits. It could be only by practical experience of this sort that one could solve satisfactorily the problem of total recovery of urine from the male rabbit, an animal endowed with a "stream" like a fire hose.

In advocating the educative value of a practical training in the intimate details of research I must not be taken as minimising the value, indeed the absolute necessity, of an adequate number of research technicians in the elaborate research projects which the solution of many problems demands. It is, however, essential that members of such research teams have a background of practical experience without which supervision of the work of the technicians is impossible.

For many trainee specialists a suitable investigative exercise will consist of an analysis of some grouping of case-records with a view to evaluating some suspected ætiological factor, the significance of a symptom or sign, the result of a certain therapeutic measure, or the illumination of the natural history of a disease process. Such an essay can be particularly valuable, since the discipline acquired is such as can be applied in later life, such research being specially suitable for the busy clinician who can only snatch an hour here and there. To be of value, though, it has to be well done, for a great deal of harm has resulted from the uncritical assembly of information selected by biased methods from fundamentally inaccurate records. It is particularly in this type of investigation that testing statistically and thinking quantitatively is so essential.

A clinical department proposing to provide research of this type requires a considerable accumulation of full and accurate case-records supported by relevant radiographs, histological preparations, and tissue blocks. At present there are relatively few units, even among the teaching hospitals, in which the case-records are of any value for this purpose. It needs careful planning and constant supervision by senior members of staff to ensure an adequate standard of records. In addition a hospital or group of hospitals requires a statistical department which will, in collaboration with the clinicians, ensure uniformity of practice and the codifying of information by modern methods which will ensure speedy and semi-automatic access to any desired group of cases. At the same time such statistical departments can never compensate for faulty original observation; the quality of the records is utterly dependent on conscientious and careful work in the consulting-room, ward, and laboratory. If I had to name the aspect of clinical work which should come first in a programme of reform, I would unhesitatingly select the preparation and preservation of case-records. Whatever be the merits and demerits of the National Health Service, the prospect it holds of nation-wide individual health-records meets with universal approval.

REPORTS ON RESEARCH

Whether the trainee be destined for a career in academic medicine or in the practice of a clinical specialty, the preparation of a report on his research problem is an important item in his education. In a small minority of instances this will be of sufficiently high standard to merit submission for publication. It is futile to expect that many will reach this standard; it must be evident from a perusal of current medical literature that a considerable proportion of the material that appears in print shows little evidence of scientific method and contributes little if anything to the sum total of knowledge. It is certain that the development of systematic training in investigative methods will greatly raise the standard of medical literature and will lighten the labours of editorial boards. A substantial proportion of these reports will be suitable for submission for the higher degrees of M.D. and M.S. Universities are showing an increasing tendency to award these degrees on the basis of evidence of having done original research or having applied the scientific method to a problem in medicine or surgery, using these terms to embrace virtually the whole field of human biology. Interpreted in this way these qualifications cease to be repetitions of the membership and fellowship and become tests of rather different attributes.

Most people have much to learn in the preparation of such reports. It is extraordinary how universal is the tendency to confuse quantity with quality and to think that any paper or thesis must be lengthy to be good. Economy of words, both spoken and written, is just as important as the economy of material resources; the slogan "Time is money" is as true in the library and the laboratory as in the factory and warehouse. I urge students to write papers as if they were reporters cabling a story at a shilling a word. The report should begin with a concise enunciation of the problem, and should then give the design of experiment in sufficient detail to make it possible for others to repeat the work. An account of the results should be followed by a discussion of the conclusions in the light of relevant previous work. Illustrations must be clear and to the point. Quantitative data require tabulation, and graphic correlation should be used whenever possible. Masses of data, though often better relegated to an appendix, must be sufficiently full to enable others to fully confirm or refute the deductions made by the author. References must be accurately listed, and abbreviations should follow those of the *World List of Scientific Periodicals*. Some years ago the *Journal of Physiology* issued a very useful pamphlet entitled "Suggestions to Authors," which is still in print and can be obtained from the editor, at the Physiology Laboratory, Cambridge, or consulted in the journal.

An essential attribute of those charged with the encouragement and direction of research is buoyant enthusiasm; a cold hypercritical destructive impatience with the immature efforts of students inevitably blights the work of any educational organisation. Scientific criticism there must be, but the student who is in difficulties—and good students and promising investigators are always in difficulties—needs encouragement and must be made to feel that his failures are necessary and indeed desirable steps to success. Emerson was right when he said that "Nothing great was ever achieved without enthusiasm."

FUNDAMENTAL RESEARCH

It is hard to discuss the subject of research without touching on the question of fundamental as opposed to applied investigation. Some use these terms as if they had a precise meaning and were a basis for satisfactory classification. In so far as all good science strives to interpret phenomena in terms of first principles it follows that all good research is fundamental irrespective of the problem; the question of whether the answer is immediately applicable to some circumstance of our environment becomes a secondary consideration. I suspect that a common basis for the use of these terms, in a mutually exclusive sense, implies "fundamental" as such as to have no practical use. This is an unfortunate and artificial differentiation and can be avoided by the closest possible coöperation between clinicians and laboratory workers; such a collaboration reaches its maximum when these activities are combined in one and the same person. There must be moments in the life of all clinical investigators when the desire to pursue with single-minded devotion a particular research engenders some intolerance of the responsibilities of routine care of patients and teaching, but a brief pause for reflection brings a realisation that, without the stimulus of close contact with individual problems of health and

Digitized by Google

disease, he might soon cease to be a useful practitioner and director of research.

In this connexion it is well to meditate on the happenings in the Museum of Alexandria some 2200 years ago during the reigns of the first two Ptolemys. At that time, in that place, there occurred one of the greatest blazes of scientific discovery in the history of mankind. Euclid and Apollonius placed geometry on a secure footing, Eratosthenes calculated the size of the earth and came within fifty miles of its true diameter, Hero made the first steam engine, Archimedes made several basic physical demonstrations, and Herophilus contributed extensively to anatomy. Few of these great discoveries made any contribution to the welfare of man for over 1500 years, because at the time there existed a complete social gulf between the scientist and the artisan. This is in sharp contrast with another efflorescence of genius which occurred in Birmingham in the latter half of the eighteenth century. At that time there existed the Lunar Society, whose members included such masters of pure science and applied technology as James Watt, Matthew Boulton, Joseph Priestley, Josiah Wedgwood, Erasmus Darwin, and William Withering, under whose influence there was remarkably little delay in the application of inventive genius to practical problems.

FUTURE OF RESEARCH

It is very clear that it will be many years before there will be adequate facilities for including research experience of the type outlined in the training of all specialists. In fact the position will become satisfactory only when most of the senior practising specialists have themselves received such training and are actively educating their apprentices in scientific methods along with instruction in the purely vocational detail of their specialty. Development depends not so much on material resources in bricks, mortar, and costly apparatus—though these play a part—as on the multiplication of people whose daily practice and teaching are consciously, indeed aggressively, governed by the rigorous standards of scientific thought. This is not in any way antagonistic to the so-called "art of medicine"; indeed the needs of humanity are best served by the methods of thought and practice, in particular the habit of rigorous self-criticism, which are inherent in science.

In the first instance this type of training will of necessity be confined largely to teaching hospitals, since such habits of thought and practice require the stimulus of preclinical departments and of broad contacts with university faculties of science. One detects a tendency in certain circles to suppose in the New Order that the teaching hospitals will be exclusively engaged in the instruction of undergraduates, while postgraduate specialist training will be relegated to non-teaching or regional hospitals. Though much practical clinical experience will necessitate work in these hospitals, total isolation from the universities and their hospitals would be utterly disastrous. I suggest that the aim should be to group regional specialist centres in the closest possible geographical, organisational, and intellectual relationship to the university. Only thus will there flourish a tradition which is so aptly expressed in the quotation from Wordsworth which is the motto of the journal *Nature*: "To the solid ground of nature trusts the mind that builds for aye."

"... The ordinary citizen sees little connexion between the advance of science and the fact that he is healthy; it is, he feels, a quality that other people may lack, but is his by right of a superior heredity or habit. Ill health, on the other hand, while a fault in other people, is a misfortune in himself and a serious reflexion on the state of medical science."—Sir HENRY TIZARD, *Nature*, Sept. 11, 1948, p. 396.

STREPTOMYCIN IN NON-TUBERCULOUS INFECTIONS

SUMMARY OF A REPORT TO THE MEDICAL RESEARCH COUNCIL

CLIFFORD WILSON
M.A., D.M. Oxfd, M.R.C.P.
PROFESSOR OF MEDICINE, UNIVERSITY OF LONDON; DIRECTOR OF THE MEDICAL UNIT, LONDON HOSPITAL

IN December, 1946, the Medical Research Council appointed a committee * to arrange clinical trials of streptomycin in non-tuberculous infections, in parallel with the trials in certain forms of tuberculosis which have been organised by another committee of the council. The trials in non-tuberculous infections began at five centres in London and later were extended to eleven centres throughout the country. This report summarises the pooled results of the investigation; more detailed results will be published by individual observers.

Because of the small amounts of streptomycin available, the relative rarity of suitable cases, and the wide diversity of conditions treated, experience of most infections in which streptomycin therapy may be effective is still limited. Even when, as in *Hæmophilus influenzæ* meningitis, a reasonably large series has been studied, the distribution of cases over a large number of centres has led to unavoidable variations in case selection, therapeutic procedure, and bacteriological control. For these reasons present claims must be guarded. Nevertheless, some clear-cut results have been obtained and profitable lines for further inquiry have been indicated.

These trials have been restricted to infections resistant to other forms of therapy, in which bacteriological control of treatment has been possible. With few exceptions the infecting organism has been proved streptomycin-sensitive before treatment has been begun; occasionally—e.g., in infective endocarditis—when penicillin treatment has failed, subsequent attempts to isolate the organisms have been unsuccessful.

The chief value of streptomycin (apart from tuberculosis) lies in the treatment of penicillin-resistant infections due to the gram-negative bacilli, particularly *H. influenzæ*, *Proteus*, *Ps. pyocyanea*, and *Bacterium coli*. The clinical disorders in which treatment has been most effective are septicæmias, meningitis, urinary-tract infections, and local (superficial) infections.

H. INFLUENZÆ MENINGITIS

The results of preliminary trials in the United States suggested that streptomycin might be particularly valuable in this condition; a standard scheme of treatment was therefore recommended in the present investigation.

Dosage.—The intramuscular dosage was 20 mg. per lb. of body-weight daily in divided (four-hourly) doses; and the intrathecal dosage (in saline) was 50–100 mg. as the initial dose, according to age, and 25–50 mg. on subsequent days. Treatment was continued for at least seven days after the cerebrospinal fluid (C.S.F.) became sterile.

Results.—Streptomycin was given in 43 cases, of which 4 received in addition sulphonamides, penicillin, or serum; in 5 others the C.S.F. was reported sterile before streptomycin injections were started. Of the remaining 34 cases, the infection was controlled in 25 (74%) and treatment failed in 9. There was no significant difference in age, duration, or C.S.F. changes between the two groups, but clinically the unsuccessful cases appeared to be more

* Sir ALEXANDER FLEMING (chairman), Prof. RONALD V. CHRISTIE, Prof. L. P. GARROD, Mr. R. VAUGHAN HUDSON, Prof. H. RAISTRICK, Dr. ROBERT CRUICKSHANK, Dr. F. C. O. VALENTINE, Dr. F. R. SELBIE, and Prof. CLIFFORD WILSON (secretary).

Digitized by Google

severe. Where typing was carried out the organism was found to be Pittman type b. When treatment was successful the C.S.F. usually became sterile within twenty-four hours of the first intrathecal injection. Streptomycin was effective in 13 cases which had relapsed on other treatment, and in 9 cases in which the infection had been present for two weeks or longer; 4 patients relapsed after an initial response to streptomycin, but the organism remained sensitive and further treatment with streptomycin alone was successful. The principal cause of failure was the development of resistance by the organism; this occurred in 7 of the 9 failures, sensitivity changing from 0·5 to as high as 5000 units in 1–4 days.

From this series it appears that in *H. influenzæ* meningitis streptomycin alone is probably as effective as any other form of treatment at present available. The development of resistance is, however, a serious drawback, and it has been decided to use in future trials a combination of streptomycin, penicillin, and sulphonamides from the start.

OTHER FORMS OF MENINGITIS

Streptomycin was given in 14 cases of meningitis due to penicillin-resistant bacteria. The causal organisms included *Bact. coli*, *Ps. pyocyanea*, *Staphylococcus pyogenes*, *Proteus*, and *Streptococcus fæcalis*. In the majority of cases the meningitis developed after operation for cerebral abscess or cerebral tumour. The infection was controlled in 11 instances. Streptomycin is therefore a valuable new therapeutic agent in pyogenic meningitis due to penicillin-resistant organisms.

SEPTICÆMIAS

Streptomycin was given in 5 cases of subacute bacterial endocarditis due to *Strep. viridans* or to *H. influenzæ*, and in 1 case of uncertain nature. Except in the last-named case, the response to streptomycin has been only temporary; 2 cases of septicæmia without endocarditis, due to *Ps. pyocyanea* or to *Bact. coli*, have responded satisfactorily.

URINARY-TRACT INFECTIONS

A series of 61 patients with urinary-tract infection due to *Bact. coli*, *Ps. pyocyanea*, *Proteus*, *Staph. pyogenes*, or *Strep. fæcalis* was investigated in ten centres. In roughly half the cases the infection has been controlled by intramuscular administration of 3 g. streptomycin daily for 1–3 days. Failure was almost always due to the development of resistance. Like other antibacterial agents, streptomycin has a limited value where there is some underlying condition which is liable to lead to recrudescence of the infection.

LOCAL SEPSIS

Streptomycin was given to 55 patients with local infections, including a wide variety of lesions such as infected burns, operation wounds, superficial ulcers, sinuses, abscess cavities, and septic skin conditions. The bacterial causes were similar to those detailed in the preceding paragraph. Daily applications of a saline solution of streptomycin (2 mg. per ml.) have been used either alone or combined with intramuscular therapy. The results are favourable, particularly in superficial lesions, provided that all necrotic tissue is removed. A standard technique is essential. Streptomycin has been used effectively as a cover for skin-grafting. In a proportion of cases failure has been attributable to the development of resistance.

RESPIRATORY INFECTIONS

Chronic lung infections due to bronchiectasis and lung abscess (14 cases) have been treated by inhalation and intramuscular injection. Though a temporary reduction in the bacterial content of the sputum has been noted the cases showed little if any clinical improvement. The results of a preliminary trial in whooping-cough were inconclusive. More experience is needed of *acute* lung infections due to penicillin-resistant organisms.

INTESTINAL-TRACT INFECTIONS

Streptomycin 2–4 g. spread over seven days has been given by mouth in 42 cases of infantile diarrhœa. Sensitive organisms rapidly disappear from the gut. As the infecting agent in this condition is not always the same, it was to be expected that the results obtained in different centres would vary. Some centres report clinical benefit, but so far treatment has not been sufficiently controlled to warrant any definite conclusions. Further trials, in which streptomycin will be given to alternate cases, are being undertaken. A small number of cases of ulcerative colitis and of typhoid fever have been treated by oral and intramuscular administration with negative results.

SUMMARY

In this series of cases streptomycin has often been successful in controlling:

(1) Meningitis: *H. influenzæ*, *Bact. coli*, *Ps. pyocyanea*, *Proteus*, and *Staph. pyogenes*.
(2) Septicæmia: *Bact. coli* and *Ps. pyocyanea*.
(3) Urinary infection: *Bact. coli*, *Proteus*, *Ps. pyocyanea*, *Strep. fæcalis* and *Staph. pyogenes*.
(4) Local sepsis: *Bact. coli*, *Proteus*, *Ps. pyocyanea*, *Staph. pyogenes*, and *Strep. hæmolyticus*.

There have, however, been examples of almost every type of infection in which the micro-organisms rapidly became resistant. Courses of treatment should therefore be planned to exert the greatest possible influence from the beginning. The effect of combining streptomycin with other agents, such as the sulphonamides, is under investigation.

Owing to the short periods of administration toxic symptoms have been unusual and of slight importance. Urticarial rashes and skin irritation at the site of local application have occasionally been noted.

STREPTOMYCIN TREATMENT OF MENINGITIS DUE TO GRAM-NEGATIVE SAPROPHYTES

WALPOLE LEWIN M.S. Lond., F.R.C.S.
R. L. VOLLUM M.A., D.Phil. Oxfd

From the Department of Surgery, Radcliffe Infirmary, Oxford

MENINGITIS due to saprophytic gram-negative organisms such as *Ps. pyocyanea*, *Proteus*, and coliform bacteria is uncommon but carries a high mortality. These organisms are relatively or absolutely insensitive to penicillin; and the response to sulphonamide therapy is often unsatisfactory.

Infection usually arises as a complication of spinal analgesia (Evans 1945, Kremer 1945, Vuylsteke 1947, Davidson 1947), neurosurgical operations, or the intrathecal injection of penicillin (Botterell and Magner 1945). In wounds of the head and of the spine penicillin has been so effective in combating infections due to gram-positive organisms that the pathogenicity of these gram-negative organisms, when introduced into the subarachnoid space, has become more apparent. Thus, Lewin (1948) showed that nearly a quarter of the cases of meningitis following penetrating head wounds in the latter phases of the late war, when penicillin was freely available, were due to these organisms. Besides penetrating wounds of the head and spine and operations, a chronic infection of the ear may cause a meningitis in which these gram-negative organisms are wholly or partly responsible. Coliform meningitis occurs in infants, sometimes with a recognisable focus elsewhere in the body, but it is very rare in adults.

Digitized by Google

A preliminary report in 1946 from this department on the use of intrathecal streptomycin in meningitis was disappointing (Cairns et al. 1946); severe toxic reactions were observed, and in only 1 of the 5 cases due to gram-negative organisms did the patient recover. It was significant, however, that the solitary survivor was the only patient to receive treatment early in the infection (due to achromobacter). All of the 3 patients infected with *Ps. pyocyanea* died: in 2 treatment was begun late, when spinal block was already established and pus was present in the cerebrospinal fluid (C.S.F.); the third patient died of respiratory failure shortly after the first injection of streptomycin.

Since that date we have treated 5 further patients, and the results with purer supplies of streptomycin and earlier treatment are more encouraging: 3 recovered (2 infected with *Ps. pyocyanea* and 1 with *Bact. coli*); 1 (infected with achromobacter) died; and 1 (infected with *Proteus*) did not respond to streptomycin but recovered spontaneously.

Of these 5 patients 4 received full doses of sulphonamides during the streptomycin treatment. Though some cases of meningitis due to gram-negative organisms respond to sulphonamides, the rapidity of response to streptomycin treatment in the 3 successful cases leaves no doubt about the effective agent, but a synergistic action is not excluded. The possibilities of successful treatment of a meningitis due to gram-positive and gram-negative organisms with penicillin and streptomycin combined is illustrated by case 4.

DOSAGE

The accompanying table gives the details of the 5 cases treated. In 3 the infection followed the surgical removal of a cerebral tumour or abscess, and in 2 a chronic ear infection. Since supplies of streptomycin were short, treatment had to be confined to the intrathecal or ventricular route; but undoubtedly this should be combined with systemic streptomycin, particularly when there is an extracranial primary focus. A strength of 10,000 units * per ml. in normal saline was used, and the usual dose was 50,000 units intrathecally daily and continued, when supplies were adequate, until the C.S.F. had been sterile for four or five days. In 2 cases the intraventricular route was used as well, and in 1 case, which followed excision of a cerebellar abscess and developed a spinal block, streptomycin was injected through the cerebellar decompression into a C.S.F. loculus. With this dosage the concentration of the drug remaining in the C.S.F. twenty-four hours after the injection, though very variable, was usually well above the bacteriostatic level required for the particular organism and often five times or more higher.

RESULTS

In 3 cases (2 of *Ps. pyocyanea* and 1 of *Bact. coli* meningitis) the results were very satisfactory, the organisms disappearing from the C.S.F. after the first injection; this even obtained in 1 case of *Ps. pyocyanea* meningitis, where the patient had two relapses in three and a half months, the organisms disappearing each time after the injection of streptomycin. In 2 cases there was no improvement: 1 (*Proteus*) due to relative insensitivity to streptomycin (25 units per ml.) and probably insufficient treatment; and 1 (achromobacter) which proved fatal owing to rapidly developing resistance to streptomycin while receiving apparently adequate dosage.

TOXICITY

With the doses used no toxic effects of any kind were observed; nor was there any increase in the cell or protein content of the C.S.F. attributable to the streptomycin. The largest single dose injected into the lumbar theca and into the ventricle was 100,000 units.

* 1 unit = 1 μg. of streptomycin base.

BACTERIAL RESISTANCE

In the 2 cases which did not respond to treatment organisms were finally grown from the C.S.F. which were very resistant to high concentrations of streptomycin.

Case 1 (see table).—A man of 33 had a very chronic *Proteus* meningitis secondary to an ear infection which did not respond to large doses of sulphonamides, and on two occasions a short course of intrathecal streptomycin was given (100,000 units intrathecally daily for four days) without effect on the C.S.F. or on the clinical condition. It is unfortunate that the sensitivity of the organism to streptomycin was not tested before treatment. Two months after the second course the organism was sensitive only to streptomycin 50 units per ml. At this stage the patient began to improve slowly, and now, eight months after the onset, he is doing full work and is well, apart from mild daily headache; the C.S.F. contains only 4 cells (3 lymphocytes) per c.mm. and 40 mg. of protein per 100 ml., culture being sterile.

In this case it should be noted that neither of the two courses of streptomycin lasted longer than four days. The case illustrates that, unless treatment is effective and adequate at the beginning, the infecting organism may become resistant to all chemotherapy.

In the second case resistance to the drug rapidly developed under apparently adequate treatment.

Case 2 (see table).—A boy, aged 9 years, developed a postoperative achromobacter meningitis three days after removal of a medulloblastoma of the vermis. The organism was shown to be insensitive to penicillin but sensitive to streptomycin 10 units per ml. Treatment was begun with 50,000 units into the ventricle and 50,000 units intrathecally. Twenty-four hours later a concentration of 63 units per ml. remained in the C.S.F., and a further 75,000 units was injected. Despite this large dosage the organism was again grown from the C.S.F. next day and was now insensitive to 64 units per ml. Streptomycin 50,000 units was given daily for five days, and the drug was then stopped. During these days the C.S.F. was sterile, and the cell-count, previously 1700 per c.mm., fell to below 100 per c.mm., though the amount of protein remained high and the clinical condition was unchanged. Subsequently the organism was recovered repeatedly from the C.S.F., and the child died thirty-five days after onset of the infection. Eleven days after the beginning of streptomycin treatment the organism was insensitive to streptomycin 100 units per ml.

Whether resistance to streptomycin is acquired as a result of treatment or is a natural resistance of some of the organisms, the more sensitive ones being killed early, is not yet known, but the very rapid appearance of resistance, together with the favourable cell response in the C.S.F., with sterile cultures for several days in cases such as the one described above, suggests the latter explanation, the resistant organisms later multiplying and producing a fatal result.

RELAPSES

In this series the only case to relapse after apparently successful treatment was case 4. Here the reason was obvious and one which should be borne in mind when dealing with these infections—the presence of an inadequately treated primary focus.

Case 4 (see table).—A man, aged 51, had had a discharging left ear for twenty years. In March, 1946, he became acutely ill with symptoms suggesting a cerebellar infection. A radical mastoidectomy was performed, and later a cerebellar abscess was tapped through the mastoid wound. He slowly improved despite the formation of a cerebral fungus through the wound and two attacks of meningitis. In July he relapsed suddenly, and in August was transferred to the Radcliffe Infirmary.

On admission he had a large fungus presenting through the mastoid wound which was discharging pus from which *Staph. aureus* and *Ps. pyocyanea* were cultured. He was treated with intramuscular penicillin and daily dressings to the fungus, and this finally healed.

Digitized by Google

In October the cerebellar abscess was excised. After this excision the patient had a recurrence of the meningitis. *Staph. aureus* and *Ps. pyocyanea* were grown from the C.S.F. He improved on intrathecal and systemic penicillin and, later, sulphadiazine by mouth; but after eleven days he relapsed, both organisms were grown from the C.S.F., and a spinal block developed. Local penicillin was now given into the C.S.F. loculus which had formed beneath the cerebellar decompression, and from this site also both organisms were obtained. With this treatment the *Staph. aureus* disappeared but *Ps. pyocyanea* remained in pure culture. Streptomycin 20,000 units was now injected daily for two days, at the end of which the loculus had completely subsided.

A fortnight later the patient's temperature rose sharply to 102°F, the loculus reappeared, and once more turbid C.S.F. containing both organisms was withdrawn. After two injections of penicillin 10,000 units the *Staph. aureus* disappeared, and at this stage streptomycin 40,000 units was injected as well. All subsequent cultures were sterile, and for the next seven days penicillin 60,000 units and streptomycin 80,000 units were given daily through the loculus, which steadily diminished in size. After four days of this treatment the patient's temperature settled to normal for the first time since his operation, and he began to improve. He made a steady convalescence over the next three months and was finally discharged from hospital afebrile; the cerebellar decompression was soft, but the spinal block was still present.

He relapsed, for the third time after the excision of his abscess, a fortnight after discharge from hospital, and this time *Ps. pyocyanea* and *Strep. viridans* were grown from the loculus, which had reappeared. Once more combined therapy was successful. *Ps. pyocyanea* disappeared after the first injection of streptomycin 50,000 units, and *Strep. viridans* after the fourth instillation of penicillin. Systemic penicillin and sulphadiazine were also given. In view of this relapse Mr. G. Livingstone was consulted, who advised re-exploration of the mastoid. This was done while the patient was still on combined therapy daily. At operation a petrositis was present, and the cochlea was found to be filled with pus. Infection had been reaching the C.S.F. via the labyrinth. This operation did not cause the meningeal infection to flare up, and the patient made a steady convalescence, local streptomycin being continued this time for twenty-one days and penicillin for six days. The spinal block persisted.

The patient was seen again nine months later, when the ear was dry and there had been no recurrence of the infection.

The *Ps. pyocyanea* in this instance remained extremely sensitive to streptomycin despite the use of streptomycin on two previous occasions. This supports the view that streptomycin resistance is more likely to be natural than acquired.

COMMENT

The results in these few cases suggest that streptomycin will be of value in treating meningitis due to these gram-negative organisms. Undoubtedly the difference between these results and those of two years ago is due to purer streptomycin and earlier institution of treatment before frank pus or spinal block has developed. The activity of streptomycin is seriously impaired in the presence of pus. As Abraham and Duthie (1946) have shown, this is primarily due to the associated lowering of the pH of the medium. In addition, if the infection has reached the stage of pus formation, it may be impossible to obtain an adequate concentration of streptomycin throughout the cerebrospinal fluid path-

DETAILS OF TREATMENT WITH STREPTOMYCIN IN 5 CASES

Case no.	Age (yr.)	Source of infection	Bacteriology	Duration of meningitis before streptomycin treatment (days)	White cells per c.mm. in C.S.F. at height of infection	Streptomycin details							Ancillary treatment	Result
						Route	Largest single dose (units)	Total dosage (units)	Sterile C.S.F. obtained	Initial sensitivity of organism (units per ml.)	Concentration in C.S.F. after 24 hr. (units per ml.)	Resistance to streptomycin		
1	33	Left ear	*Proteus*	42	1400	L	100,000	700,000	Sterile during treatment but organisms grown later	..	8–25	Sens. to 50 u/ml. 2 months later	Sulphadiazine	Unchanged
2	9	Post-operative after removal of cerebellar tumour	Achromobacter	6	8500	L & V	50,000	425,000	Not obtained	10	15–63	Resistant to 64 u./ml. by 2nd day and to 100 u./ml. on 11th day	'Sulphamezathine'	Died
3	41	Post-operative after removal of cerebral abscess	*Ps. pyocyanea*	3	1650	L & V	100,000	350,000	After 24 hr.	4	8–100	..	Sulphamezathine, intramuscular penicillin (not during streptomycin therapy)	Recovered
4	51	Left ear (*a*)	*Ps. pyocyanea Staph. aureus*	25	800	Into C.S.F. loculus	80,000	640,000	After 24 hr.	..	20–40	..	Sulphadiazine, intramuscular and intrathecal penicillin	Recovered but relapsed 3 months later
		(*b*)	*Ps. pyocyanea Strep. viridans*	5	1000	Into C.S.F. loculus	50,000	1,000,000	After 24 hr.	..	20–40	..	Sulphadiazine, intramuscular and intrathecal penicillin	Recovered
5	4	Post-operative after removal of cerebellar tumour	*Bact. coli*	1	3500	L & V	75,000	450,000	After 24 hr.	3	5–20	..	Sulphadiazine, intramuscular penicillin	Recovered

1 unit = 1 μg. of streptomycin base. L = lumbar theca. V = ventricle.

Digitized by Google

ways since collections of purulent exudate and debris will prevent free diffusion of antibiotics. These were probably the main factors in the failure of streptomycin to save the 2 cases of *Ps. pyocyanea* meningitis reported previously (Cairns et al. 1946). For these reasons alone, early treatment before pus forms is a vital factor in successful treatment.

This point was emphasised recently in the treatment of a postoperative infection beneath the scalp flap of a patient with an old gunshot wound of the head. A small abscess cavity beneath the scalp contained about 10 ml. of pus, which grew a penicillin-sensitive hæmolytic streptococcus and a resistant *Staph. aureus*. The streptococcus quickly disappeared with local instillation of penicillin, but the *Staph. aureus* remained and was resistant to penicillin 65 units per ml. but sensitive to streptomycin 1·25 units per ml. Over the next five days a total of 260,000 units of streptomycin was injected into the cavity. At the end of this time pus could still be aspirated which was very acid in reaction, *Staph. aureus* was still present, and the sensitivity to streptomycin was unchanged. The local concentration of streptomycin must have been many times the bacteriostatic level, yet there was absolutely no response. The pus was subsequently drained with rapid subsidence of the infection.

The appearance of resistant strains of the organism is another important factor in deciding the success or failure of streptomycin therapy, and it is most important to ensure that the initial doses are sufficiently large. Moreover, though the doses used here give an adequate concentration in the C.S.F. over twenty-four hours for the very sensitive organisms, there are often well-marked differences in streptomycin levels in the C.S.F. twenty-four hours after injection in the same patient. Thus, one patient after 100,000 units given intrathecally showed a concentration of 25 units per ml. remaining in the C.S.F. twenty-four hours later; yet a similar dose next day gave only 8 units per ml. after twenty-four hours. It is therefore essential not only to test the sensitivity of the organism before beginning treatment, so as to ensure an adequate initial dosage, but also to check C.S.F.-streptomycin levels during treatment.

Fortunately these infections, though severe, are usually not fulminating, and in the present state of our knowledge it is wise, where possible, to begin treatment with sulphadiazine and defer streptomycin treatment until the sensitivity of the organism has been tested in vitro. Sulphadiazine is effective in some cases. With an organism sensitive to concentrations up to 10 units per ml., streptomycin should be injected intrathecally daily in doses of 50,000–100,000 units and continued until the C.S.F. has been sterile for at least five days. When the causal organism is relatively insensitive, higher C.S.F.-streptomycin levels can be obtained by intrathecal injections twice or thrice daily. When supplies are available, systemic streptomycin should also be given not only to deal with other foci of infection but also because streptomycin passes the blood-C.S.F. barrier in appreciable quantities, particularly in acute meningitis.

Lack of response to streptomycin treatment in a meningitis due to a sensitive gram-negative organism may be due to (1) inadequate dosage, (2) developing resistance (or resistant strains) of the organism, (3) an untreated primary focus, or (4) pus formation.

We wish to thank Sir Hugh Cairns for his advice in the preparation of this paper.

REFERENCES

Abraham, E. P., Duthie, E. S. (1946) *Lancet*, i, 455.
Botterell, E. H., Magner, D. (1945) *Ibid*, i, 112.
Cairns, H., Duthie, E. S., Smith, H. V. (1946) *Ibid*, ii, 153.
Davidson, I. M. (1947) *Ibid*, ii, 653.
Evans, F. T. (1945) *Proc. R. Soc. Med.* 39, 181.
Kremer, M. (1945) *Brit. med. J.* ii, 309.
Lewin, W. (1948) *Brit. J. Surg.* 35, 266.
Vuylsteke, C. A. (1947) *Brit. med. J.* i. 179.

STREPTOMYCIN IN PULMONARY TUBERCULOSIS

REPORT ON TEN CASES

R. Y. KEERS
M.D. Edin., M.R.C.P.E., F.R.F.P.S.
MEDICAL DIRECTOR, RED CROSS SANATORIA OF SCOTLAND

THE value of streptomycin in the treatment of meningeal and miliary tuberculosis having been established, its properties in other forms of tuberculosis are now being explored. Such reports as have appeared, mainly in America, suggest that streptomycin may have an almost specific effect on tracheobronchial tuberculosis (Brewer and Bogen 1947, Canada 1947, Parnal et al. 1947), and a beneficial effect on laryngeal tuberculosis (Black and Bogen 1947, Shamaskin et al. 1947) and intestinal tuberculosis (Sweany 1947), while Hinshaw et al. (1946) reported encouraging results in the treatment of draining sinuses of tuberculous origin. The results in purely pulmonary lesions are much less definite, but at least temporary improvement has apparently followed its use in some cases of predominantly exudative disease (Shamaskin et al. 1947, Cassidy and Dunner 1947, Allison and Nilsson 1947).

Opportunities for the clinical study of streptomycin in Britain have so far been limited, but as supplies are likely to increase in the near future an account of a very small series of cases treated during the first half of 1948 may be of interest.

Through the generosity of the American Red Cross a consignment of 600 g. of streptomycin was presented to the Scottish Red Cross Sanatorium at Tor-na-Dee early this year. The selection of suitable cases for treatment required much thought, for this generous gift had to be utilised to the greatest advantage. The cases selected were (1) a severe tracheobronchial tuberculosis, (2) a tuberculous chest-wall sinus persisting after a thoracoplasty for tuberculous empyema, (3) two cases of acute exudative pulmonary tuberculosis, and (4) a small contralateral spread of disease following thoracoplasty. The remaining streptomycin was used as a cover during the stages of thoracoplasty operations in cases in which there seemed to be an appreciable risk of extension of the disease.

Dosage.—All cases received 1 g. of streptomycin in the twenty-four hours, given in two doses of 0·5 g. at 8 A.M. and 8 P.M. Administration was by intramuscular injection and no local application of the drug was tried.

CASE-RECORDS

Case 1.—A man, aged 43, was admitted in November, 1946, with a year's history of cough, sputum, and loss of weight. His sputum was T.B.-positive and a radiogram of his chest showed infiltration in the upper and mid zones of the left lung, with tomographic evidence of cavitation. "Roof-tiling" of the ribs over the affected area, with deviation of the trachea to the left, suggested a widely adherent apex and was accepted as a contra-indication to artificial pneumothorax. Left upper thoracoplasty was considered to be the treatment of choice. Four weeks after admission, however, there was radiological evidence of extension of the disease in the left lung, with the formation of a new cavity in the mid zone, this being rapidly followed by a further spread of the disease to the lower zone. This was accompanied by increased cough and sputum and a deterioration in the patient's general condition. Brief febrile bouts occurred, associated with a complete cessation of sputum. Major surgery was contra-indicated meantime, and a left phrenic crush, supplemented by pneumoperitoneum, was carried out. Some benefit ensued and the X-ray appearance improved, with gradual clearing of the fresh infiltration in the lower lung field. This benefit was only temporary; the cough increased in severity, developing a harsh brassy note, febrile episodes with sputum retention

Digitized by Google

recurred, and the cavitation in the left upper and mid zones became increasingly obvious. The whole clinical picture now suggested tracheobronchial tuberculosis, which was confirmed by bronchoscopic examination in June, 1947, when extensive ulceration of the left main bronchus was seen.

It was now a question of marking time until streptomycin became available, and the status quo was maintained with some difficulty until April, 1948, when the American supply was received. On April 13 a further bronchoscopy was carried out, when œdema of the carina was noted, with ulceration on the left side. Granulations were present in the left main bronchus almost to the level of the carina.

A course of streptomycin was begun on April 16. Within a fortnight there was a well-marked improvement in symptoms, the severity of the cough had diminished, sputum was decreasing, and the patient's general condition was improving rapidly. Bronchoscopy on May 14 showed a remarkable clearing of the bronchial lesions, with healing of the ulcerated areas. The improvement was so dramatic that it was decided to proceed with the thoracoplasty operation, and the first stage was carried out on May 25, the second and third following on June 8 and 29. There were no postoperative complications. Bronchoscopy on July 8 showed some hyperæmia of the left main bronchus, with few granulations. Streptomycin was stopped on July 24, when 100 g. had been given.

The patient has continued to improve in all respects; sputum is diminishing steadily in amount and is now T.B.-negative on direct examination, and X-ray examination shows a satisfactory collapse of the left lung following the thoracoplasty.

Case 2.—A man, aged 25, was admitted in February, 1947, with a limited lesion in the right upper zone, where a small cavity was visible behind the clavicle. A right artificial pneumothorax was begun shortly after admission and adhesion section was carried out some 5 weeks later. Immediately after the adhesion section the patient developed a very acute pleural effusion, with high fever and much constitutional disturbance. Attempts to secure pulmonary re-expansion were defeated by very rapid pleural thickening: the fluid became turbid, contained many lymphocytes, and was T.B.-positive on guineapig inoculation. Intensive aspiration was continued until November, 1947, by which time the patient's general condition had sufficiently improved to permit obliteration of the pleural space by thoracoplasty, and the operation was accordingly done in December, 1947. There was a stormy convalescence which caused considerable anxiety and subsequent progress was slow, but X-ray examination indicated that the desired obliteration of the infected pleural cavity had been secured. A sinus, however, formed at the lower end of the operation scar and continued to discharge over a period of weeks. Bacteriological examination of this discharge showed tubercle bacilli, and typical tuberculous tissue was demonstrated in a biopsy specimen from the sinus wall. The sinus itself was about 5 in. long and showed no tendency to heal.

A course of streptomycin was begun on April 20, 1948, and 14 days later a definite improvement was noted in the sinus, which appeared to be closing. This was confirmed by injection of iodised oil. Subsequent progress was steady and uninterrupted, final healing being recorded on June 2. The streptomycin was continued until June 18, when a total of 60 g. had been given.

The patient was discharged from the sanatorium on July 20 in excellent general condition, free from all chest symptoms, and with the tuberculous sinus firmly healed.

Case 3.—A man, aged 27, arrived at the sanatorium in October, 1946. His general condition was extremely poor, he was grossly anæmic, and X-ray examination showed extensive infiltration involving the upper halves of both lungs but without any notable degree of cavitation. The larynx was severely involved, with gross œdema and infiltration of the epiglottis and arytenoids. He complained also of severe diarrhœa, and barium examination showed an advanced colitis which was accepted as tuberculous. The prognosis was regarded as very bad and the patient was kept on strict bed-rest and voice rest for many months. The anæmia proved so intractable as to raise the question of a tuberculous infection of the bone-marrow, but this could not be confirmed by sternal puncture, and eventually a response was obtained to a series of small blood-transfusions. The intestinal lesion responded also to intensive treatment with intravenous calcium gluconate and a high-vitamin diet, and by May, 1947, the alimentary function was completely normal and the patient was gaining weight. Meantime the pulmonary lesion was showing evidence of healing, but the situation in the larynx was thoroughly unsatisfactory, there being now ulceration of the epiglottis with involvement of both vocal cords. A course of calciferol was given, which for a time produced some improvement but which had to be terminated eventually owing to symptoms of intolerance. The laryngeal disease then remained static for some months but began to deteriorate again in February, 1948. Meantime the pulmonary disease had steadily improved, the sputum was T.B.-negative, and the patient's general condition was reasonably good.

The retrogression of the laryngeal condition prompted the use of streptomycin, which was begun on April 20, 1948. From that time onwards there was steady improvement. Swelling and œdema subsided, the lesions of the vocal cords cleared rapidly, and by the beginning of July healing was practically complete, apart from two small ulcerated areas in the epiglottis which were dealt with by the electrocautery. By July 23 a total of 90 g. of streptomycin had been given and the course was terminated.

The patient was discharged from the sanatorium in August, final X-ray examination having shown complete hardening of the infiltration in both lungs, while what little sputum remained was T.B.-negative both on concentration and on culture.

Case 4.—A man, aged 26, was admitted on Jan. 14, 1948, with a history of an acute febrile illness 8 weeks previously. An X-ray film of his chest at that time had shown an area of exudative disease in the right upper and mid zones. On admission his general condition was rather poor, he was mildly febrile, and his sputum, although very limited in amount, was T.B.-positive. An X-ray film of his chest suggested that there had been some clearing of the infiltration on comparison with the film taken at the outset of the illness. After a month's bed-rest, however, there was evidence of extension of the disease, accompanied by a sharp rise in the erythrocyte-sedimentation rate (E.S.R.) from 5 mm. to 25 mm. in one hour. A right phrenic crush and pneumoperitoneum were carried out, but only a very moderate elevation of the diaphragm resulted, because of adherence between the liver and diaphragm in the posterior half. Four weeks later there had been no improvement, the patient was still febrile and was tending to lose weight, and the exudative lesion in the right lung was gradually extending.

A course of streptomycin was begun on April 20 and was continued until July 28, a total of 100 g. being given. There was no evidence of any benefit from the treatment. The patient remained mildly febrile throughout, he lost 6 lb. in weight, and comparison of radiograms at the beginning and end of the course showed that, if anything, there had been some extension of the infiltration during the period.

Case 5.—A man, aged 22, was admitted on May 17, 1948. His admission was regarded as an emergency and was arranged at the special request of a Service hospital where the patient had arrived gravely ill with acute pneumonic tuberculosis. His transfer to the sanatorium was effected by air ambulance and he was so seriously ill on arrival that only the minimum of investigation was possible. He was taken straight from the ambulance to the X-ray department, where a film of his chest was obtained as he lay on the stretcher. He appeared desperately ill, with high fever up to 105°F each evening, heavy sweating, and a severe and racking cough accompanied by abundant purulent sputum which contained very numerous tubercle bacilli. His X-ray film showed extensive exudative disease in the upper half of the right lung, with ragged areas of cavitation. The lower three-fifths of the left lung was consolidated throughout.

Treatment with streptomycin was begun immediately, and a few days later a left phrenic paralysis and pneumoperitoneum were added, because the situation seemed so desperate that every possible aid must be utilised. During the succeeding fortnight there was little change. The temperature remained high and the racking cough continued, but there was no further deterioration in his condition, in contrast to the week before admission. Then slowly the tide began to turn. The temperature came down gradually to 101° and then to 100°F. He began to gain weight, the cough improved, and the sputum diminished. The radiological appearances, however, remained unaltered, despite the notable improvement in symptoms and general condition, until July 22, when for the first time the radiogram showed a moderate degree of clearing of the infiltration in the right lung and of the consolidation in the left.

Digitized by Google

By this time a total of 66 g. of streptomycin had been given. The pneumoperitoneum had been maintained gently throughout but no attempt had been made to achieve maximum elevation, owing to the severity of the patient's illness and the difficulty of fluoroscopic control.

At the time of writing his progress has been well maintained; his temperature is now normal and it seems possible that he will yet become a candidate for further collapse therapy, with the prospect of securing eventual control over the disease.

Case 6.—A man, aged 24, had a left upper thoracoplasty carried out in the sanatorium in March, 1948, to deal with a fairly extensive area of infiltration involving the upper third of the left lung, where there was tomographic evidence of cavitation. Artificial pneumothorax was not possible because of a previous left pleural effusion of some severity. After the second stage of the operation a small area of infiltration appeared in the upper zone of the right lung, which had previously been clear. The appearance of this infiltration coincided with a rise in the E.S.R. to 20 mm. in one hour.

A course of streptomycin was begun immediately, and a month later, when a total of 30 g. had been given, the lesion in the right lung had cleared completely and the E.S.R. had improved to 1 mm.

The patient has since gone ahead steadily; he is now up and about for several hours daily and should be ready for discharge in about 2 months' time.

Cases 7, 8, 9, and 10.—The balance of our supply of streptomycin was used to provide cover during the stages of thoracoplasty in four cases in which there was thought to be an unusual risk of complications. In two of these there was damage to the lung base as a result of previous pleural effusions, while the remaining two had impaired diaphragmatic function owing to a delayed recovery of movement following phrenic-crush operations. Streptomycin was given in a dosage of 1 g. daily for 96 hours before and after each stage of the operation. All four cases pursued a smooth and uncomplicated course throughout.

No *complications* or *side-effects* which could be attributed to the streptomycin were noted in any of the cases.

DISCUSSION

A report on a small series of diverse cases such as these must be regarded as of interest rather than of value, but it may help in suggesting the type of case which is likely to derive most benefit from this antibiotic.

The response of the bronchial disease, the chest-wall sinus, and the laryngeal lesion was prompt and unmistakable, as one would have anticipated from the American reports already cited, and this suggests that streptomycin will find its greatest sphere of usefulness in the management of the extrapulmonary sequelæ of tuberculosis.

Case 4, an active pulmonary lesion of exudative type, was very disappointing. American experience had suggested that some benefit might have been expected in such a case, and one had hoped that, by using streptomycin to control the exudative phase, the patient might have been fit for thoracoplasty fairly soon. As it is, the course of the illness has not been shortened in any way.

The case of tuberculous pneumonia (case 5), on the other hand, did appear to benefit appreciably and conformed to the experience of Allison (1947) in that the fever and constitutional symptoms subsided early, while radiological improvement was delayed for some weeks.

The part played by the streptomycin in case 6 and in the four thoracoplasty cases in which it was used prophylactically is impossible to assess. The small contralateral lesion in case 6 might well have resolved spontaneously.

CONCLUSIONS

The decision to use streptomycin in any case of pulmonary tuberculosis should be taken only after most careful consideration. The benefit to the patient is by no means certain, and this possible benefit must be weighed against the danger of producing a streptomycin-resistant strain of bacilli in a particular case and thus creating a future public-health problem. On the available evidence there appear to be very few purely pulmonary cases in which the use of streptomycin could be advised.

This very limited experience with streptomycin suggests that it may have a definite value in the treatment of the extrapulmonary complications of pulmonary tuberculosis.

Its use in tuberculous pneumonia, to prepare the way for effective collapse therapy, is probably justified in view of the high mortality associated with this form of the disease.

My thanks are due to the American Red Cross, whose generous gift of streptomycin made the treatment of these cases possible, and to Mr. F. J. S. Gowar, F.R.C.S., and Mr. E. G. Collins, F.R.C.S., for carrying out the bronchoscopic and laryngeal examinations.

REFERENCES

Allison, S. T. (1947) *Amer. Rev. Tuberc.* **56**, 401.
— Nilsson, J. M. N. (1947) *Ibid*, p. 579.
Black, M., Bogen, E. (1947) *Ibid*, p. 405.
Brewer, L. A., Bogen, E. (1947) *Ibid*, p. 408.
Canada, R. O. (1947) *Ibid*, p. 508.
Cassidy, W. A., Dunner, E. (1947) *Ibid*, p. 552.
Hinshaw, H. C., Feldman, W. H., Pfuetze, K. H. (1946) *Ibid*, **54**, 191.
Parnal, C., Brock, B. L., Moyer, R. E. (1947) *Ibid*, **56**, 565.
Shamaskin, A., Morris, L. C., Des Autels, E. J., Mindlin, J., Zvetina, J. R., Sweany, H. C. (1947) *Ibid*, p. 540.
Sweany, H. C. (1947) *Ibid*, p. 415.

THE EOSINOPHIL CELL

STUDIES IN HORSE AND CAMEL

FREDERIC DURAN-JORDA
M.D. Barcelona
DIRECTOR, PATHOLOGY DEPARTMENT, ANCOATS HOSPITAL, MANCHESTER

WHILE investigating the secretion of red blood-cells by eosinophils I was interested to learn that the eosinophils of the horse contained granules resembling small red blood-cells (Dr. Leandre Cervera, personal communication). Arrangements were therefore made for a thorough study of the blood and other tissues of the horse, and from this it was found that the granules of the eosinophils in the peripheral blood were far larger than those found in various other mammals, including man. The granules varied in size from cell to cell, some of them being as large as a small red blood-cell (fig. 1). On micro-incineration the granules left ashes behind, as happens with the granules in man. A study of the gastric and intestinal mucosa of the horse showed that, as in the other herbivora, the eosinophils arose from those organs where the red blood-cells appeared to be secreted in situ (fig. 2), a phenomenon similar to that described for the abomasum of different hervibora (Duran-Jorda 1945). In the spleen of the horse were very many eosinophils, in some of which the granules were as large as small red blood-cells.

In spite of my being able to show objectively the secretion of the red blood-cells by the eosinophils in

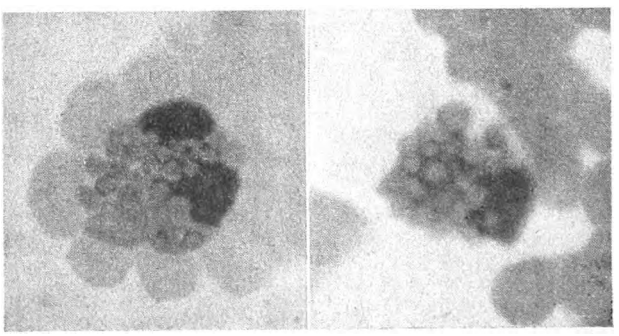


Fig. 1—Horse's blood showing granules of different sizes, some like small red blood-cells, in eosinophils.

Digitized by Google

hervibora and in man, it has been objected that the cells were really undergoing phagocytosis, and that the huge cells containing about 200 red blood-cells found in the thyroid gland in man (Duran-Jorda 1947) were the result of an unknown mechanism of cellular degeneration (*Lancet* 1947).

It was decided that the point could be proved more conclusively if it was demonstrated with red blood-cells of a characteristic shape, and for this reason the camel was chosen, because it has elliptical red cells. The idea was to demonstrate that the granules contained in the eosinophils of this animal had the same characteristic appearance as the free red cells. The scientific director of the local zoo provided us with the camel blood; and, since the peripheral blood contained a large quantity of eosinophils, the observations were simple. Smears stained with May-Grünwald-Giemsa showed that all the granules contained in the eosinophils were elliptical.

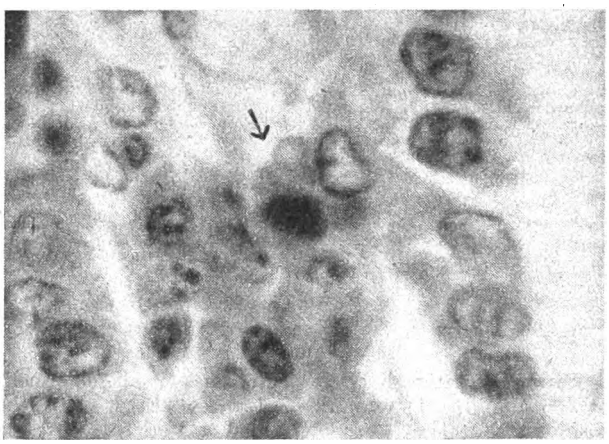


Fig. 2—Gastric mucosa of horse showing eosinophils in situ secreting red blood-cells.

They were smaller than those of the horse but larger than those of man, and it was most satisfactory to be able to find this elliptocytosis in the granules both while they were contained in the cell and after they had broken out of the cytoplasm by the action of smearing. The granules in the eosinophils of the peripheral blood (fig. 3) showed a definite range of sizes, but even at their largest they were never so big as those found in the horse. If the granules can grow larger in the cells, one can imagine their expulsion into the circulating blood as perfectly developed red cells.

In contrast to the elliptical granules of the eosinophils were the normoblasts, which were round (fig. 4). According to the accepted ideas of blood formation these normoblasts should be denucleated by some unknown process or should undergo either karyorrhexis or expulsion

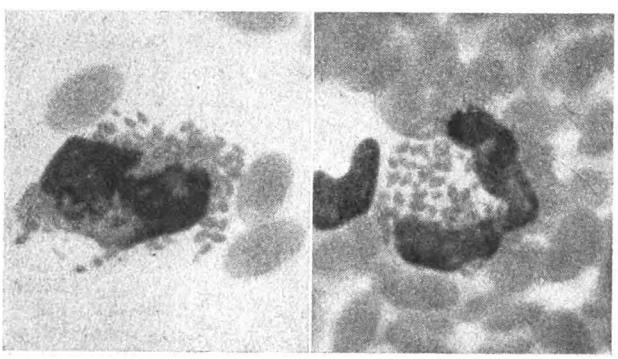


Fig. 3—Camel's blood showing different sizes and elliptical shape of intracellular and extracellular granules.

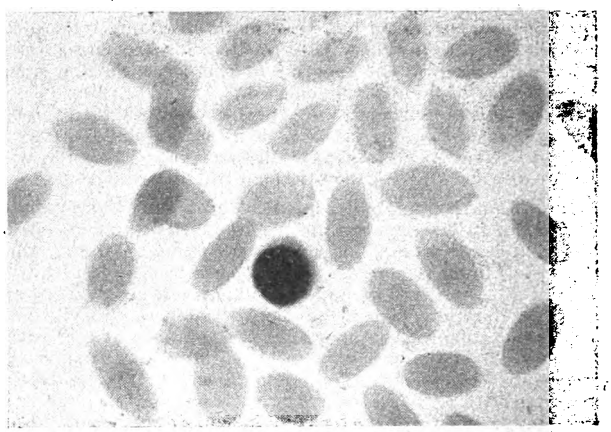


Fig. 4—Normoblast in camel's blood. Note surrounding elliptical red blood-cells.

and, in the case of the camel, should afterwards transform themselves into elliptocytes, the process being so laborious that it is difficult to accept. The elliptical granules of the eosinophils in camel's blood are in striking contrast to the granules of the basophils, which are perfectly circular (fig. 5).

Owing to the difficulty of obtaining camel tissues, I have not yet had the opportunity of studying the gastric and intestinal mucosa and spleen to find the missing link in the complete cycle of blood formation in this animal; but, if such tissues are forthcoming, it should be simple enough to show that the eosinophil is the mother cell of the "mere hæmoglobin-freighted drops of protein" (Thompson 1942). For hæmatologists

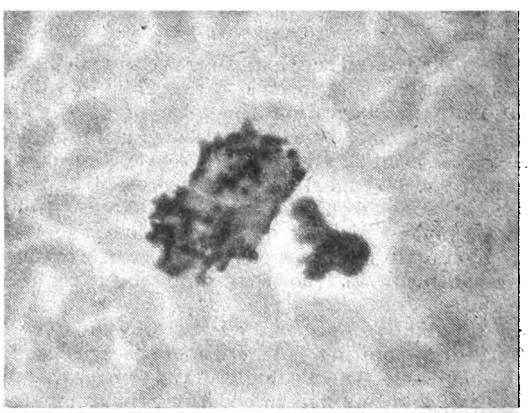


Fig. 5—Camel's blood showing basophil leucocyte containing circular granules.

who prefer a different interpretation there is the alternative one that the eosinophil is a product of a monstrous phagocytosis of about 200 red blood-cells which are carefully shrunk until they become eosinophil granules (von Kölliker 1853).

My thanks are due to Dr. Leandre Cervera for his enthusiastic interest and helpful suggestions on these problems; Inspector Wilfred Taylor, C.R.S.I., for his coöperation in supplying veterinary specimens; and Mr. Gerald Iles, zoological superintendent of Belle Vue, Manchester, without whose assistance the investigations on camel's blood would have been impossible.

REFERENCES

Duran-Jorda, F. (1945) *Vet. J.* **101**, 191.
— (1947) *Nature, Lond.* **159**, 293.
Lancet (1947) i, 414.
Thompson, D. W. (1942) On Growth and Form. London; p. 435.
von Kölliker, A. (1853) Manual of Human Histology. London vol. ii, p. 148.

Digitized by Google

MENINGO-ENCEPHALITIS IN MAN DUE TO THE LOUPING-ILL VIRUS

GEORGE DAVISON
M.D. Durh., M.R.C.P., D.C.H.
ASSISTANT PHYSICIAN, CHILDREN'S DEPARTMENT, GENERAL HOSPITAL, NEWCASTLE-UPON-TYNE

CHARLES NEUBAUER
M.D. Vienna
DEPUTY MEDICAL SUPERINTENDENT, CITY HOSPITAL, NEWCASTLE-UPON-TYNE

With Serological Report by

E. WESTON HURST
D.Sc., M.D. Birm., F.R.C.P.
HEAD OF SUBDIVISION OF MICRO-ORGANISMAL RESEARCH, IMPERIAL CHEMICAL (PHARMACEUTICALS) LTD.

LOUPING-ILL occurs naturally in sheep on hill farms in certain areas of Scotland and the border counties of England, where it is responsible for a considerable mortality. Well known to farmers for over a century, it has, because of its economic importance, been the subject of much discussion and investigation, culminating in 1930–32 in a series of reports in which its nature and mode of transmission were finally established. Pool et al. (1930), in successful experimental transmission, showed that louping-ill is due to a filter-passing virus, and MacLeod and Gordon (1932) established that the sheep tick (*Ixodes ricinus*) is the natural vector. Further studies on its histopathology and transmission to other animals were made by Hurst (1931), Brownlee and Wilson (1932), Gordon et al. (1932), and Findlay and Elton (1933), from whose communications the following information on louping-ill in animals is taken.

LOUPING-ILL IN SHEEP

Direct infection from sheep to sheep does not occur; infection is conveyed by the tick, *Ixodes ricinus*, which in its larval stage becomes infected by sucking the blood of an infected sheep, and is itself infective in its nymphal and adult stages.

When a sheep is bitten by an infected tick, there is usually an incubation period of one or two days followed by a simple febrile reaction lasting three or four days. There is then a short afebrile period, after which the temperature again rises and typical symptoms develop. The sheep becomes dull and incoördinate, and there are muscular tremors, especially of the head, with salivation and champing of the jaws. Often the sheep makes leaping movements (hence the name "louping-ill"), and there may be ataxia of cerebellar type. Within a period varying from a few hours to one or two days the sheep becomes unable to stand, and it lies, usually on one side, kicking vigorously. Paresis of one or more limbs may ensue, and this stage is succeeded, usually in a few hours, by coma and death.

Occasionally the sheep dies in the initial febrile period of a septicæmic type of illness and without nervous signs. Other sheep develop only the initial febrile upset and then recover completely, being thereafter immune against further attacks. In examinations of sheep from farms where the disease was prevalent 20% were found to be immune, presumably having survived an infection.

There is a second tick-borne infection of sheep, "tick-borne fever," which is immunologically distinct from louping-ill, and it is stated that only when the sheep already has tick-borne fever does infection with the louping-ill virus lead to the characteristic cerebral illness.

Sheep may be infected experimentally by inoculation of the virus intracerebrally and by other routes. When experimental inoculation is successful, the disease as described above follows after an incubation period of one or two days. Repeated passage of the virus from sheep to sheep by intracerebral inoculation appears to heighten its virulence and shorten the incubation period.

At necropsy of sheep dying of either natural or experimental louping-ill there are no gross changes, but histological examination shows a general meningo-encephalo-myelitis, with varying degrees of damage to the Purkinje cells in the cerebellum and often severe damage to the nerve-cells in the medulla and spinal cord. No inclusion bodies can be seen. The virus can be recovered from the blood of experimentally infected sheep between the third and seventh days after inoculation; after death it can be recovered constantly from the brain, and often from other tissues.

LOUPING-ILL IN OTHER ANIMALS

Though the disease does not appear to occur naturally in other animals, many, including the pig, mouse, field vole and monkey, can be infected experimentally by intracerebral inoculation, and the mouse can be infected also by intranasal instillation. Full accounts of the clinical and pathological findings in the pig, mouse, and monkey are given in the communications already mentioned. Briefly, in all these animals infection leads to a meningo-encephalo-myelitis; the symptoms and the intensity and distribution of the histological changes vary from species to species. Inclusion bodies have been described in the mouse and the monkey.

LOUPING-ILL IN MAN

Rivers and Schwentker (1934) reported in detail illnesses suffered by 4 persons working with the louping-ill virus in the laboratory. Their sera were examined, after recovery, for virus neutralisation by a technique fully described by Rivers and Schwentker. All 4 sera neutralised the virus of louping-ill. Similar tests were made on 46 people with, or recovered from, various illnesses; in only 1 was there any virus neutralisation, and this was incomplete. In 10 other people who had possibly had contact with louping-ill virus these serological tests were negative. Finally, of the sera of 3 persons who had handled the virus but gave no history of illness, 1 neutralised the virus and 2 did not. From these results it was concluded that the test gave reliable evidence as to whether or not a person had been infected with the virus. Consideration of the circumstances under which the 4 people fell ill, and of the features common to their illnesses, led to the conclusion that these illnesses were due to infection with the virus of louping-ill.

Wiebel (1937) and Wesemeier (1938) each reported a further case in a laboratory worker, with serological confirmation of diagnosis, and in Wesemeier's case the result of the serological test was rendered more significant by the observation that a year previously a virus-neutralisation test on the patient's serum had been negative.

In one of the 6 patients the illness would have passed for influenza; in the remaining 5 it took the form of a meningo-encephalitis, and in 3 of these was biphasic, the meningo-encephalitic phase following an "influenzal" phase after several days' comparatively good health. The symptoms and findings included headache, prostration, fever, vomiting, drowsiness, insomnia, photophobia, diplopia, slow speech, vertigo, tremors, ataxia, neck stiffness, bradycardia, and papillœdema. All patients recovered completely in one to three months. The cerebrospinal fluid (C.S.F.) was examined in 4 of the 6 patients; in 1 it was normal, whereas in 3 the protein-level was raised and there was lymphocytosis. The 4 persons reported by Rivers and Schwentker were all engaged in performing intranasal instillations of the virus into mice, and in 1 the onset of symptoms was within eight days of beginning work with the virus.

All 6 reported cases of human louping-ill have been in laboratory workers, and the present cases are the first in which infection is assumed to have been acquired naturally and outside of the laboratory.

Digitized by Google

CASE 1

A man, aged 47, usually in excellent health. Twenty years previously he had had an attack of double vision, said to have been corrected with spectacles. In the war of 1914–18 he had had T.A.B. inoculation. In 1938 a small tumour had been excised from a finger, and in 1939 a "crop of boils" had troubled him. Otherwise he had not required medical attention.

From time to time his diagnostic work on animals had involved handling the virus of louping-ill, but the last time had been on June 16, 1945, when he had inoculated six mice with preparations from the brain of a sheep suspected of having had louping-ill; none of the mice had succumbed.

From Aug. 18 to 25, 1945, he was concerned with sheep-dipping at Buttermere. Some sheep were infested with *Ixodes ricinus*, and he brushed several nymphs from his arms but did not note any bites. On Aug. 25 he returned home to Newcastle-on-Tyne and felt as if he had a slight chill. Next day he had a mild conjunctivitis and felt thirsty. On the 27th he felt better in the morning, but the sensation of chill returned in the afternoon, and in the evening his temperature rose to 100°F. On the 28th he felt rather "heavy," but he attended a meeting in the afternoon. In the evening he was off his food and went early to bed. On the 29th he was a little worse, but still attended to his duties. On the 30th his morning temperature rose to 102°F, he felt chilly and stayed in bed, and was thirsty but unable to eat.

He remained bedfast and was seen on Aug. 31 and Sept. 1 by Dr. T. H. Bates and Dr. L. Richmond, who found only a high temperature with relatively slow pulse. Blood sent for a Widal test to Dr. Emslie Smith, of the Public Health Laboratory in Newcastle-upon-Tyne, gave no agglutination above the titre which could be expected from the previous T.A.B. inoculation.

Improvement began on Sept. 2, the ninth day of illness, and his temperature fell to normal on Sept. 4. From the 5th to 9th he got up daily, though feeling rather weak. On the 9th he developed a severe headache and vomiting. From then until his admission to hospital a week later he had variable frontal headache, at times intense fever, intermittent vomiting, and constipation. His pulse remained slow, and no focal signs were elicited.

On Sept. 16, the eighth day of the second phase of the illness and three weeks from the onset of the initial symptoms, he was admitted to the Newcastle General Hospital.

On admission he looked unwell but not seriously ill. He was alert but but showed evidence of a severe headache, lying on his side with hands to his head when not disturbed. From time to time he vomited small quantities of bile-stained fluid. His pulse was full and regular; the pulse-rate was 60 per min. at first, but fell later in the day to 52; temperature 100°F. His skin felt hot and moist; his tongue was moist, with a thick white fur. His throat was clear, and his ear drums grey and glistening. The superficial lymph-nodes were not enlarged. There was a little generalised abdominal tenderness, but no distension or rigidity. The descending colon was palpable, but neither liver nor spleen could be felt. No abnormal signs were detected in heart or lungs. His neck was not stiff. The pupils were very small, but equal and reacting normally. Because of the small pupils, his optic fundi were not clearly seen. White-cell count 10,000 per c.mm. (eosinophils 4%, basophils 1%, neutrophil polymorphs 73%, lymphocytes 16%, monocytes 6%); Wassermann reaction negative.

Next morning he seemed a little better, but in the evening he vomited three times and complained of severe headache. Late in the evening he was flushed, and his speech was a little rambling. Temperature did not exceed 99·6°F.

On Sept. 18 the patient's condition caused concern; headache and vomiting persisted, with mental confusion (reaction-time and facial expression betrayed difficulty in answering simple questions). No neck stiffness; no Kernig's sign. Pupils still small, equal, and normally reacting. No cranial-nerve weakness. Optic discs, seen for first time, were moderately swollen. Knee-jerks and plantar reflexes unobtainable; abdominal reflexes active and equal. Temperature did not exceed 99·2°F.

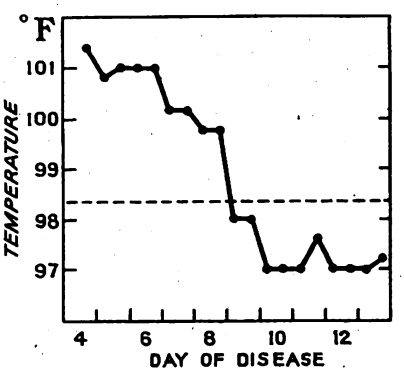
On the 19th lumbar puncture produced clear fluid under pressure of 180 mm. water and containing protein 0·04 g. per 100 ml., a trace of globulin, and 17 lymphocytes per c.mm. Cerebral abscess having been tentatively diagnosed, a course of intramuscular penicillin 12,500 units three-hourly to a total of 50,000 units was started, followed by a course of sulphadiazine by mouth to a total of 26 g. in seventy-two hours.

From the 18th to 21st his symptoms still caused considerable anxiety, but on the 22nd he was improving. His headache and vomiting ceased, and the patient began to eat, sit up, and read. Optic fundi normal. From then on improvement was steady. Temperature fell to normal and remained so. The pulse-rate which had ranged from 54 to 72 per min. since admission began to rise and reached normal on Dec. 2. On the 24th lumbar puncture produced fluid under pressure of 30 mm. water (60 mm. after jugular compression) and containing protein 0·04 g. per 100 ml. and 80 cells, nearly all lymphocytes, per c.mm. On the 28th C.S.F. was obtained with great difficulty and only after jugular compression; a cell count again showed 80 cells, mostly lymphocytes, per c.mm. By end of September the patient was well, apart from occasional slight headache and weakness. He returned home on Oct. 7 and has since remained well.

Comments.—The febrile part of this man's illness took place chiefly before his admission to hospital. Radiograms of chest and skull were within normal limits. There is no reason to believe that the course of the illness was affected by treatment with penicillin and sulphadiazine.

CASE 2

A farmer, aged 59, was admitted to the City Hospital for Infectious Diseases, Newcastle-upon-Tyne, on Sept. 3, 1947, with a provisional diagnosis of meningitis. He had spent his life on farms in the Border area of Northumberland, and had for the past three and a half years worked on a farm near Bellingham in western Northumberland. For more than ten years before this he had been on a farm only a few miles distant. Before 1947 he had enjoyed excellent health.



Temperature chart of case 2.

In May, 1947, he began to lose his appetite, especially for meat, and to lose weight, his clothes becoming too large for him. His bowels, previously regular, became costive. His symptoms persisted, and at the end of the haymaking season he felt unexpectedly tired and a little breathless. Towards the end of August he felt very tired, but travelled to a sale on Aug. 28, and to the shoemakers, some distance away, next day. He spent Aug. 30 at home, and on the 31st his head ached and his neck became stiff. He got up as usual on Sept. 1 but felt very giddy and had to return to bed at midday. Throughout the afternoon he remained in bed, but after tea became feverish and delirious, got up from his bed, and left the house in his underwear. He was brought back to bed and retained there with some difficulty. Dr. G. W. L. Kirk, of Bellingham, saw him at 5.30 P.M., when his temperature was 103°F, and attributed the symptoms to work in the hot sun. Throughout the night the patient sweated profusely and became incontinent of urine, this incontinence persisting at intervals through the following days. Next day he was quieter and did not try to leave his bed. His temperature fell to 100°F, and he dozed for most of the day. In the morning of Sept. 3 his temperature had risen to 102°F, and he was still drowsy. In the afternoon he again became delirious and could not be kept in bed. Dr. Kirk found definite neck stiffness, but could not elicit any other abnormal sign, and he tentatively diagnosed meningitis.

On admission the patient was very ill. His appearance was plethoric, and a good physique was marred by wasting. Though fully conscious he appeared rather deaf. After answering questions rationally he became confused and rambling. He left his bed and tried to walk on to the ward balcony. His temperature was 101°F and pulse-rate 84 per min. His tongue was dry and furred. He resisted palpation of his abdomen; the liver and spleen could not be felt. Physical examination of heart and lungs revealed no abnor-

Digitized by Google

TABLE I—C.S.F. FINDINGS IN CASE 2

Date	Naked-eye appearance	Pressure	Cells			Protein (g. per 100 ml.)	Globulin	Sugar (g. per 100 ml.)	Chlorides (g. per 100 ml.)
			No. per c.mm.	Polys %	Lymphos %				
Sept. 3	Slightly turbid	Increased	848	81	19	0·07	+	0·07	0·67
Sept. 5	Hazy	..	410	75	25	0·11	+	0·05	0·66
Sept. 8	Clear	Normal	104	9	91	0·09	+	0·00	0·69
Sept. 23	..	..	35	3	97	0·05	+	0·07	0·70
Nov. 6	..	..	0	..	..	0·04	±	0·07	0·70

mality. His arteries were tortuous and thickened; his pulse was regular, full, and bounding; blood-pressure 134/76 mm. Hg. There was well-marked neck stiffness, but Kernig's sign was negative. The pupils were very small but normally reactive, and the cranial nerves were normal. No paralysis or paresis was evident in his limbs, and the deep reflexes were present and equal. The abdominal reflexes could not be elicited, and the plantar reflexes were doubtful, there being a brisk withdrawal reflex. All night the patient was very restless, often trying to leave his bed, and next day his condition showed little change. His neck was still very stiff, and he resented interference. Temperature 101°F. He took fluids well without vomiting. Though still able to answer questions, he would afterwards mumble unintelligibly.

By Sept. 5 his condition had deteriorated, though his temperature had fallen to 100°F. He was semi-comatose and incontinent of urine and fæces. The tone in the right arm was increased, with deep reflexes more brisk than on the left. The plantar responses were extensor. On Sept. 6 and 7 his condition was grave, with semi-coma, stertorous breathing, continuing incontinence of urine and fæces, pronounced neck stiffness, cog-wheel rigidity of the limbs, and, in the night, Cheyne-Stokes breathing; his temperature remained at 100°F.

On the 8th the fever ended by crisis, and the patient appeared not so gravely ill. His muscular rigidity was less and he was more alert though he again tried to leave his bed. In the next few days the slight improvement continued, but he remained incontinent of urine and fæces, and some muscular tremors became apparent. On the 10th the optic fundi was first seen clearly; the margins of both discs were blurred, though no swelling was apparent. On the 11th he answered questions but with slurred speech, and he remained restless and confused, sometimes trying to get out of bed, up to Sept. 15.

TABLE II—NEUTRALISATION TESTS WITH SERUM OF CASE 1

Dilution of virus	Mortalities in groups of 6 mice			
	Patient's serum		Horse serum	
	1st test	2nd test	1st test	2nd test
	Intracerebral inoculation			
10^{-7}	0	0	1	3
10^{-6}	Not done	0	Not done	6
10^{-5}	0	2	5	6
10^{-4}	Not done	3	Not done	6
10^{-3}	6	6	6	6
10^{-2}	6	Not done	6	Not done
	Intramuscular inoculation			
10^{-7}	0	..	Not done	..
10^{-5}	0	..	5	..
10^{-3}	0	..	5	..
10^{-2}	1	..	6	..

By Sept. 18 he was much improved and was continent of urine and fæces. His muscular rigidity had gone, but the deep reflexes remained brisk, and there was slight intention tremor. Improvement continued over the next few weeks. By Oct. 25 he had gained some weight and was cheerful and coöperative. He was no longer deaf. He could not remember the onset of his illness or the first few days in hospital. His optic discs were flat, but the outline remained blurred on the left side. The pupils remained very small but they reacted normally, and no other abnormality of the cranial nerves was detected. There was a well-marked tremor in the upper limbs, and some increase in tone; power and coördination were good; the deep reflexes were active and equal, and sensation was normal. The abdominal reflexes were present and equal. There was a little increase in tone in the lower limbs, with good power and coördination; the knee-jerks were exaggerated and equal, and the ankle-jerks present and equal, without clonus; the plantar responses remained extensor; sensation was normal. The patient could walk without support but he was ataxic and showed rombergism.

TABLE III—NEUTRALISATION TESTS WITH SERUM OF CASE 2

Dilution of virus	Mortalities in groups of 6 mice							
	Patient's serum			Serum M		Serum G	Horse serum	
	9th day		23rd day					
	1st test	2nd test	2nd test	1st test	2nd test	1st test	1st test	2nd test
10^{-6}	S,S,S, S,S,S	S,S,S, S,S,S	S,S,S, S,S,S	5,5,6, 6,6,S	6,7,7, 7,7,7	6,6,6, 6,6,9	6,6,6, 6,9,9	7,7,8, 9,10,S
10^{-4}	5,13,18, S,S,S	6,7,9, S,S,S	12,12,12, S,S,S	5,5,5, 5,6,6	x,5,7, 7,7,7	5,5,6, 6,6,6	5,5,5, 5,5,5	6,7,7, 7,7,7
10^{-3}	5,5,5, 5,6,6	7,7,7, 7,7,7	7,7,7, 8,8,S	5,5,5, 5,5,5	6,7,7, 7,7,7	x,5,5, 5,5,5	5,5,5, 5,5,5	6,7,7, 7,7,7

The numerals indicate the days of death of individual mice.
x, non-specific death. S, animal survived.

On Nov. 12 the patient was discharged from hospital, ten weeks after his illness had begun. Most of the signs of his illness had then left him, but he walked with a slight stoop and did not swing his right arm; his right plantar response remained extensor. Speech and expression were normal.

The patient's temperature during the first ten days in hospital is shown in the accompanying figure; he was afebrile after that. The C.S.F. findings are given in table I; the fluid was on all occasions sterile on culture. A Lange colloidal gold test, done on the last specimen, gave 5555432000.

Treatment consisted solely in general nursing measures and the administration of nicotinic acid, thiamine, and ascorbic acid.

SERUM-NEUTRALISATION TESTS

Blood was collected from case 1 on Oct. 19, the 55th day after onset of symptoms, and from case 2 on Sept. 9 and 23, the 9th and 23rd days. Dr. E. Weston Hurst reported on these sera as follows:

"The sera were mixed with various dilutions of a louping-ill virus of known titre. After standing for half an hour at room temperature the mixtures were inoculated intracerebrally or intramuscularly into groups of 6 mice each weighing about 20 g. As a control, similar dilutions of virus were mixed with normal horse serum, and in case 2 with two other human sera (M and G) under examination for neutralising properties against other viruses. In each case two tests were performed, with essentially similar results.

"Table II indicates definite neutralisation of the virus by the serum of case 1. The intramuscular tests show neutralisation of much stronger suspensions than do the intracerebral, but in both series of tests the results are sufficiently clear-cut. Table III presents similar data for the serum of case 2; in this case the mixtures were inoculated only intracerebrally. Again the serum neutralises virus, and the results suggest that the second sample is rather more active in this respect.

"The presence of antibodies in these two sera may be taken as proof that the donors had been infected with the

Digitized by Google

virus of louping-ill. In case 1 the presumption is that the recent severe nervous illness represented this infection. In case 2 evidence for connecting the recent nervous symptoms with infection by the virus is rather stronger, inasmuch as the neutralising properties of the serum had apparently increased in the interval between the first and second bleedings.

"The serum of case 2 did not neutralise the virus of lymphocytic choriomeningitis. It did, however, possess neutralising power against the virus of herpes febrilis, a not uncommon property of human sera."

COMMENTS ON CASES

Dr. Hurst's findings show that case 1 had passed through an infection with the louping-ill virus before October, 1945. The symptoms described conform closely to those previously reported for cases of louping-ill in man. Moreover, case 1 had previously had no illness, however slight, which could have been attributed to louping-ill infection. There are therefore good grounds for assuming that the present illness was the result of infection with the louping-ill virus.

The descriptions of the other human cases are compatible with an incubation period of a few days, comparable with the incubation period in animals, naturally or experimentally infected. Case 1 had had no laboratory contact with the virus for several months, but, within a few days of the onset of his illness, he had been infested with *Ixodes ricinus* from sheep in an area where louping-ill occurs. It seems reasonable to conclude that his present illness was the result of infection transmitted by the tick bite.

In case 2 the evidence that the present illness was louping-ill naturally acquired is even more conclusive. Again there was no history of any previous illness which could have been attributed to the louping-ill virus, and an apparent rise of the protective power of the serum during the illness suggests that the tests were made during the period of infection. Laboratory infection can be excluded. The illness differs from that in any previously reported case in its severity and in the probability that the patient will be left with permanent sequelæ. This may be linked with the observation that the C.S.F. showed a continued pleocytosis and increase in globulin for at least two months and a paretic Lange curve after eleven weeks. Case 2 did not contract the illness until he was 59, though he must have been exposed to the risk of infection for many years. Perhaps poor health, as shown by the loss of energy, appetite, and weight for some months previously, had increased his susceptibility to infection.

DISCUSSION

Louping-ill in man bears comparison with other virus infections of the central nervous system, such as poliomyelitis, and with the illness in animals. The illness in man and in the sheep show many points of resemblance such as the biphasic character, meningeal reaction, and cerebellar signs. The fact that cases of louping-ill in man other than those infected in the laboratory have not previously been recorded is probably due to failure of diagnosis rather than lack of cases. The diagnosis might well be made more often were the clinical picture more widely known.

The clinical picture of louping-ill in man is probably as variable as that of poliomyelitis. It is now known that the classical picture of paralytic poliomyelitis is one of the less common manifestations of the infection, which is often followed by only a mild non-specific illness with rapid recovery; the same may be true of louping-ill. Nevertheless, recognition of louping-ill will depend primarily on recognition of the cerebral type of illness. It is therefore justifiable to try to paint this picture in the light of the limited number of cases so far recognised.

A few days after laboratory exposure to the virus, or after tick bite in an endemic area, the illness begins with malaise, headache, and fever, which continue for about a week. There is then an afebrile interval of one or two weeks, during which the patient gradually recovers and may return to work. The symptoms now return with increased intensity—severe headache with fever, vomiting, bradycardia, drowsiness, insomnia, confusion, and possibly tremors and ataxia. Physical signs are relatively few but may include neck stiffness, papillœdema, and cranial-nerve palsies. The fever abates in a few days, and the symptoms have largely cleared in a week, but a few weeks elapse before the patient feels fully recovered. During the second phase the blood shows a mild leucocytosis of 10,000–12,000 per c.mm., with 70–80% neutrophils. Lumbar puncture yields a clear or slightly blood-stained fluid, with a normal or slightly raised protein content and a pleocytosis of 50–500 cells per c.mm., predominantly lymphocytes.

Variations of this picture so far known are that the illness may be mild, ending with the first phase and without development of meningo-encephalitis; or the first phase may be wanting and the second phase more severe, with widespread cerebral involvement causing tremors, ataxia, and pyramidal signs, and leading to permanent sequelæ. The cells in the C.S.F. may initially be polymorphs.

The disease should be suspected whenever meningo-encephalitis develops in a person exposed to the louping-ill virus either in the laboratory or by contact with sheep ticks in one of the endemic areas, especially in the summer. The diagnosis may be confirmed by virus-neutralisation tests properly carried out and interpreted by an expert. A diagnosis might be made by animal inoculation of blood removed at the onset of the illness, but it is extremely unlikely that the diagnosis would be considered at that stage.

In case 1, when papillœdema was found, especially in view of the bradycardia and increasing symptoms, a cerebral tumour or abscess was suspected, though no primary focus for an abscess was found. The records were searched to find if the tumour excised from a finger seven years previously might have been of a type which could metastasise later to the brain, but it proved to have been benign. Finally, as recovery ensued, meningo-encephalitis of unknown origin was diagnosed, and it was the patient who offered the diagnosis which was ultimately accepted. In case 2 the clinical and C.S.F. findings led to the diagnosis of a virus infection of the central nervous system, and consideration of his occupation and of the area from which he came promoted the investigation of his serum.

The relationship of louping-ill to Russian spring-summer encephalitis remains to be considered. The intensive work on this disease in Russia in 1937–39 has been summarised by Somorodintsev (1944). The illness he describes shows striking resemblances to louping-ill. It is a virus disease transmitted by *Ixodes persulcatus* and is transmissible to monkeys, goats, sheep, and mice and other rodents. It is believed that birds and rodents act as a natural reservoir. In man infection produces a severe meningo-encephalitis, with a mortality of 20–30%, and with frequent residual paralyses. Whereas louping-ill is seen commonly in sheep and uncommonly in man, Russian spring-summer encephalitis is common in man; in each case the mortality is high in the host commonly affected. Russian spring-summer encephalitis differs from louping-ill in the incidence of residual paralyses. Casals and Webster (1943, 1944) have studied the viruses of louping-ill and Russian spring-summer encephalitis in relation to other viruses which affect the central nervous system. They have found, by complement-fixation, neutralisation, and cross-resistance tests on susceptible animals, a very close relationship between the viruses of louping-ill and of Russian spring-summer encephalitis, but no relationship with any other viruses

Digitized by Google

known to affect the central nervous system. The serum of a patient who had recovered in 1933 from louping-ill gave positive complement-fixation and neutralisation tests with the viruses of both louping-ill and Russian spring-summer encephalitis, as did the serum of a patient who had an encephalitic illness while working with the two viruses in the laboratory. There is therefore, according to Casels and Webster, a striking similarity between the two viruses in their clinical effects, modes of transmission, and immunological responses.

SUMMARY

Two cases of louping-ill in man are reported, with evidence suggesting that the infection was acquired naturally and not in the laboratory as in previous cases.

The clinical picture of louping-ill in man is that of meningo-encephalitis, usually following a prodromal influenza-like illness and followed by complete recovery in most cases.

It is suggested that the illness would be more often diagnosed if it were suspected whenever a meningo-encephalitis appears in a person exposed to louping-ill virus.

The evidence linking louping-ill with Russian spring-summer encephalitis is given.

The credit for diagnosis in case 1 lies essentially with the patient, Mr. William Lyle Stewart, of the Department of Agriculture, King's College, Newcastle-on-Tyne. To him we are indebted also for a clear history of his symptoms, for advice on how the diagnosis could be established, and for sources of further information.

Thanks are also due to Dr. W. S. Walton, medical officer of health for Newcastle-upon-Tyne, and to Dr. George Hurrell and Dr. E. G. Brewis, medical superintendents of the Newcastle General Hospital and the City Hospital for Infectious Diseases respectively, for facilities provided; Dr. R. Norton and Dr. Emslie Smith for bacteriology; Mr. G. F. Rowbotham for neurosurgical advice; Dr. S. Whately Davidson for radiological reports; Dr. W. H. H. Merivale for biochemistry; Dr. Paul Szekely for helping one of us (G. D.) with translation of the literature; and Dr. T. H. Bates, Dr. L. Richmond, and Dr. G. W. L. Kirk for reference of the patients and information given.

REFERENCES

Brownlee, A., Wilson, D. R. (1932) *J. comp. Path.* **45**, 67.
Casals, J., Webster, L. T. (1943) *Science*, **97**, 246.
— — (1944) *J. exp. Med.* **79**, 45.
Findlay, G. M., Elton, C. (1933) *J. comp. Path.* **46**, 126.
Gordon, W. S., Brownlee, A., Wilson, D. R., MacLeod, J. (1932) *Ibid*, **45**, 106.
Hurst, E. W. (1931) *Ibid*, **44**, 231.
MacLeod, J., Gordon, W. S. (1932) *Ibid*, **45**, 240.
Pool, W. A., Brownlee, A., Wilson, D. R. (1930) *Ibid*, **43**, 253.
Rivers, T. M., Schwentker, F. F. (1934) *J. exp. Med.* **59**, 669.
Somorodintsev, A. A. (1944) *Amer. Rev. Soviet Med.* **1**, 400.
Wesemeier, K. (1938) *Dtsch. Arch. klin. Med.* **182**, 451.
Wiebel, H. (1937) *Klin Wschr.* **16**, 632.

LEONTIASIS OSSIUM

C. BERKELEY WAY
M.C., M.B. Lond.
MEDICAL OFFICER, HENDON COTTAGE HOSPITAL, LONDON

WITH the improvements that have taken place in dentistry and in the surgery of the nasal accessory sinuses, cases of leontiasis ossium should become rare. The skull from the case reported here has been accepted by the museum of the Royal College of Surgeons.

The patient was a spinster, who died in 1944 at the age of 73. Her appearance and health were normal until the age of 20, when she had a bicuspid tooth stopped. She had no pain, but a few months afterwards a hard swelling developed in the gum above the tooth, followed later by similar changes in the cheek. Much dental treatment followed, but the swelling steadily increased, spreading to the other cheek and into the frontal region. Beyond occasional headaches the condition caused her no physical or social inconvenience. She was a charming, witty, and well-beloved lady who continued her work as a book-keeper until four months before her death, with only one short period of ill health.

In 1939 she had a transient hemiplegia: blood-pressure 220/95 mm. Hg; left knee-jerk exaggerated and left plantar reflex extensor; otherwise no physical signs. She was working again in six weeks, the left knee-jerk remaining slightly greater than the right and the left plantar reflex indefinite until her death. The B.P. continued high, and there was some cardiac enlargement. Four months before her death she left her office well, but later was found crawling up the stairs to her flat. From then onwards muscular control slowly left her; deafness, which had not been present before, became intense; and her mental faculties were much slowed. However, if one could wait, she would eventually provide a witty and appropriate answer to a question. Swallowing became difficult, hypostatic congestion supervened, and she died in coma.

Fig. 1—"Lion-like" head of patient with leontiasis ossium.

Her nares and intranasal spaces were wide, but there was no crusting. She never had a cold. Her ear drums were normal. Bone conduction was lost. Her mandible was not unduly small in comparison with her sister's. Radiogram of the pelvis was normal. For the condition of the skull see figs. 1 and 2.

Fig. 2—Anteroposterior and lateral radiograms of skull.

COMMENTS

In view of the hyperpiesia, it can be fairly said that the condition caused little inconvenience to her health and was only slightly contributory to her death.

The history appears to follow the usual lines in that a chronic septic osteoperiostitis follows a sinus infection and one by one the accessory air chambers are filled with masses of inflammatory cancellous bone protruding outwards and causing great disfigurement. Bony changes spread to the skull (cancellous hyperostosis of Virchow); the mandible sometimes is involved, but the base of the skull usually escapes. In the present case, however, the base is involved and the mandible is normal. The lion-like head is well depicted in the photograph. The absence of colds and the dryness of the nose suggest that the mucosa lining the sinuses is the major source of nasal secretion.

"... Can there be values greater than the mere attainment of health? One reason why we have not been more successful in directing people toward healthful living is that subconsciously many have decided, and quite correctly, that there are more important things than merely being healthy."
—W. W. BAUER, M.D., director, bureau of health education, American Medical Association, in Motivation in Health Education. London, 1948; p. 20.

Digitized by Google

Reviews of Books

Acute Intestinal Obstruction

RODNEY SMITH, M.S., F.R.C.S., assistant surgeon, St. George's Hospital, London. London: E. Arnold. 1948. Pp. 259. 18s.

GREATER knowledge of the pathology of acute intestinal obstruction has led to much improvement in the results of treatment. This monograph is a timely exposition of the subject. Mr. Smith discusses the pathology, diagnosis, and treatment of acute obstruction and gives an account of the technique of treatment by intubation, and of the nature of the changes in body fluids caused by stoppage of the bowels. A well-illustrated description of the use of radiology in diagnosis is contributed by Dr. Eric Samuel. Every known cause of obstruction, from the level of the pylorus to the anus, is covered, and the book is a reference work which can be well recommended to all surgeons.

Eat and be Healthy

Diets and Nutrition in Ceylon. LUCIUS NICHOLLS, C.M.G., M.D. Camb., sometime director of the Ceylon Bacteriological Institute. Colombo: Associated Newspapers of Ceylon. 1947. Pp. 69. 5s. 8d.

ALL those who have come across Dr. Nicholls's work on nutrition in Ceylon will be keen to see his synthesis of the subject of diet and will look forward to reading this book. They will not be disappointed. Though, or perhaps because, he has adopted a simple style, his words often have dramatic power. For example: "Some classes of Mohammedan women in Egypt and India practise strict purdah, whereby they spend their lives in closely guarded dwellings; many of these women cannot afford milk, butter, or ghee. Ignorant of the values of fish-liver oil, they become afflicted with osteomalacia, and may become so deformed that they are unable to give birth to a child—pregnancy means death to them." It must not be thought that this book is useful only to the Sinhalese, or to governors and governed in tropical countries. It is also important to those who live in more temperate climates. The diets of native races which are strange to us often throw light on our own dietary problems, as witness the works of Stefánsson on the Eskimos and of Orr and Gilks on the Kikuyu and the Masai, not to mention more recent work by Professor Platt. The problem of nutrition is the same all over the world, though the local solutions may be different.

Principles of Occupational Therapy

Editors HELEN S. WILLARD, B.A., O.T.R., director of the Philadelphia School of Occupational Therapy; CLARE S. SPACKMAN, B.S., M.S. in ED., O.T.R., director of the occupational therapy department, University of Pennsylvania Graduate School of Medicine Hospital. Philadelphia and London: J. B. Lippincott. 1947. Pp. 416. 25s.

THE technique of occupational therapy has a growing literature, but far too little attention has been directed towards the underlying principles. How often one hears occupational therapy described as being either diversionary or remedial in purpose, as if that were all. Actually, it has many more important functions: it can be employed as a valuable aid to diagnosis, in the investigation of neuroses and psychoses; it can help to determine activity tolerance, in the treatment of chronic medical disorders; it can help in the restoration of physical and nervous function, imperilled by severe illness or injury; it can provide a useful stimulus to the creative faculty, for patients confined to long periods of inactivity, and help to counter the obsessional anxiety and antisocial tendency of the psychologically disturbed; and it can actually form part of the prevocational testing and vocational training of those who need to change their employment because of serious and permanent disability. The methods by which these uses can be served in different medical and surgical disorders, in the treatment of mental disease, and in the reablement and education of crippled children, of the blind, the tuberculous, and the arthritic, are well described in this volume, though it is more strictly a handbook of occupational therapy than a treatise on principles. Valuable hints are given on the right way to approach a patient ("try to untangle his fears and provide him with incentives"), on the best methods of instruction, and on the types of occupational therapy suited to various disorders.

The book is almost confined to occupational therapy as taught and practised in the United States, where, it appears, there are now 21 schools, almost all connected with university medical centres, and an average of 1750 new students each year, each of whom takes a university course or is already a graduate. Probably because of their preoccupation with American methods the authors do not refer to the incorporation of occupational therapy in industry itself, as carried out so successfully in Birmingham and Luton; to the use of art therapy, as in the British Red Cross Picture Library scheme; or to Mr. John Colson's valuable book on occupational-therapy technique.

Juvenile Delinquency in an English Middletown

HERMANN MANNHEIM, reader in criminology, University of London. London: Routledge and Kegan Paul. 1948. Pp. 120. 12s. 6d.

Dr. Mannheim has turned to advantage the war-time evacuation of his university department to Cambridge; though his choice of title may seem a little damping to those who consider Cambridge atypical. The work follows on the important "Cambridge Evacuation Survey," and is an ecological study of the records of 109 pre-war and 123 war-time delinquent boys placed on probation or under supervision. True to modern statistical tradition, the author is a severe critic of his own material: the records are incomplete, compiled by many agencies and with no thought of a possible research value; numbers are few and there is no control group; and anyway, statistics based on court cases are more intimately related to the quality of the local police activity than that of the delinquent child. Such drawbacks have deterred less determined investigators, but the work is painstakingly done and (except that groups of 10 or less are reduced to percentages) is a sound object lesson in method for the research student.

The principal findings, as might be expected from such material, are cautious and modest, useful for comparison with other studies and as confirmation rather than original. The recommendations are wise and farsighted, but derive more from the author's vast experience than from the present study. Dr. Mannheim does not effectively answer by this study critics of *Young Offenders* who held that, in this field, there is little future for the method of statistical investigation and that the urgent need is still for individual inquiry into the psychodynamics of delinquency.

The Report of the ROYAL SOCIETY EMPIRE SCIENTIFIC CONFERENCE, held in June-July, 1946, has now been published. Besides the papers given at the conference the two volumes contain reports of the discussions, the recommendations made, and accounts of the origin and conduct of the conference, and of the opening ceremony. (Edinburgh: Printed for the Royal Society by Morrison & Gibb. 1948. Pp. 828 and 707. Two vols. 42s.)

Taylor's Principles and Practice of Medical Jurisprudence (10th ed. Vol. I. London: J. & A. Churchill. 1948. Pp. 723. 45s.).—Few reference books can claim the reputation that "Taylor" has maintained in both English and Scottish courts since the first edition appeared in 1863; this first volume of the 10th edition has been revised on a broad scale. Prof. Sydney Smith has moulded these twin volumes for some 20 years, wisely retaining much of Taylor's original discursive style and shrewd observation, while revising scientific method and the ever-changing statutory law in conformity with the march of time. The authority of the text is beyond question and no review profits by a fine combing for gaps in the setting of such a vast field. Much new material —including innumerable case-reports—has been added with care and judgment. The only major mishap in production is an example of the adage that textbooks are always out of date: the Workmen's Compensation Acts were superseded on July 5 by the National Insurance (Industrial Injuries) Act of 1946 and the Law Reform (Personal Injuries) Act, 1948. The book is sound, comprehensive, couched in a fine literary style in forthright English, and displays unassailable judgment.

Digitized by Google

ARNOLD BOOKS

New and Standard Works

Surgery of the Stomach and Duodenum

By **T. H. SOMERVELL**, M.A., M.B., B.Ch., F.R.C.S., Surgeon-in-Charge, London Mission Hospital, Neyyoor, S. India. viii+546 pages, 231 illustrations, 4 coloured plates. *Just published.* **45s. net**

A fully illustrated account of this branch of surgery for general surgeons.

Acute Intestinal Obstruction

By **RODNEY SMITH**, M.S., F.R.C.S., Assistant Surgeon, St. George's Hospital, London. xii+256 pages, 101 illustrations. *Recently published.* **18s. net**

A clear account of the latest views on the subject, including the importance of suction drainage.

Gynæcological and Obstetrical Anatomy

By **C. F. V. SMOUT**, M.D., M.R.C.P., Assistant Professor, Dept. of Anatomy, and **F. JACOBY**, M.D., Ph.D., Reader in Histology, Dept. of Physiology, University of Birmingham. *Second Edition*, thoroughly revised and brought up to date. xii+248 pages, 185 illustrations, many in colour. **40s. net**

Originally published under the title of "The Anatomy of the Female Pelvis."

The Stuff We're Made Of

By **W. O. KERMACK**, M.A., D.Sc., LL.D., F.R.S., Research Laboratory, Royal College of Physicians, Edinburgh, and **P. EGGLETON**, D.Sc., F.R.S.E., Reader in Physiology, The University of Edinburgh. *Second Edition.* viii+356 pages, 74 figures, 8 plates. *Recently published.* **10s. 6d. net**

A fascinating account of biochemistry for those with only a general scientific knowledge. The new edition gives some account of the recent remarkable advances made in this relatively new field.

Surgery of Abdominal Hernia

By **G. B. MAIR**, M.D., F.R.C.S., First Assistant to Professor of Surgery, University of Durham. viii+384 pages, 137 illustrations. *Recently published.* **25s. net**

Deals fully with the surgical treatment of this common condition, with special reference to repair by skin grafts.

The Treatment of Malignant Disease by Radium and X-Rays

Being a Practice of Radiotherapy

By **RALSTON PATERSON**, M.D., F.R.C.S.E., D.M.R.E., F.F.R., Director, Holt Radium Institute, Manchester. x+622 pages, 150 illustrations. **45s. net**

A complete account of the treatment of malignant disease as practised at one of our largest centres. Details of organisation, equipment, etc., for the establishment of large or small clinics are included.

The Hair and Scalp

By **AGNES SAVILL**, M.A., M.D., F.R.C.P., Honorary Dermatologist to the Royal Surrey County Hospital, Guildford. *Third Edition.* xii+304 pages, 54 illustrations. **16s. net**

"As a treatise on disorders and diseases of the hair and scalp this volume has no equal and this new edition will be found more complete than ever before."—*Medical World.*

Hutchison's Food and the Principles of Dietetics

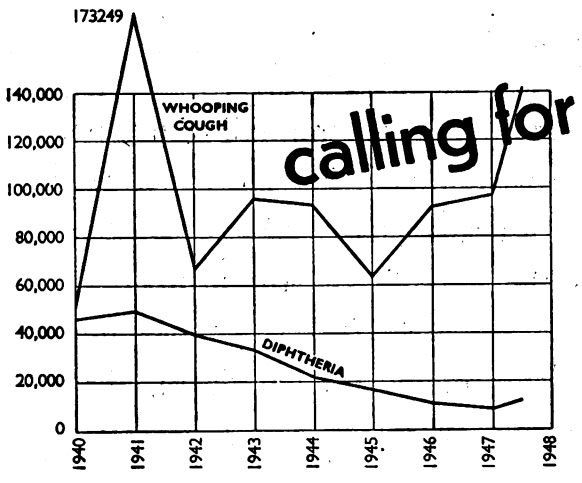
Revised by **V. H. MOTTRAM**, M.A., formerly Professor of Physiology, King's College of Household and Social Science, and **GEORGE GRAHAM**, M.D., F.R.C.P., Physician to St. Bartholomew's Hospital. *Tenth Edition.* xviii+728 pages, 28 illustrations. *Recently published.* **21s. net**

The new edition has been completely revised, the chapters on vitamins rewritten and a new chapter added on Processing and Storage of Foods.

Fully descriptive leaflets and Medical List free on request

EDWARD ARNOLD & CO.

LONDON: 41, MADDOX STREET, W.1



STATISTICS *United Kingdom figures for reported cases 1940 to June, 1948 in yearly periods from the Registrar-General's returns.*

calling for COMBINED action

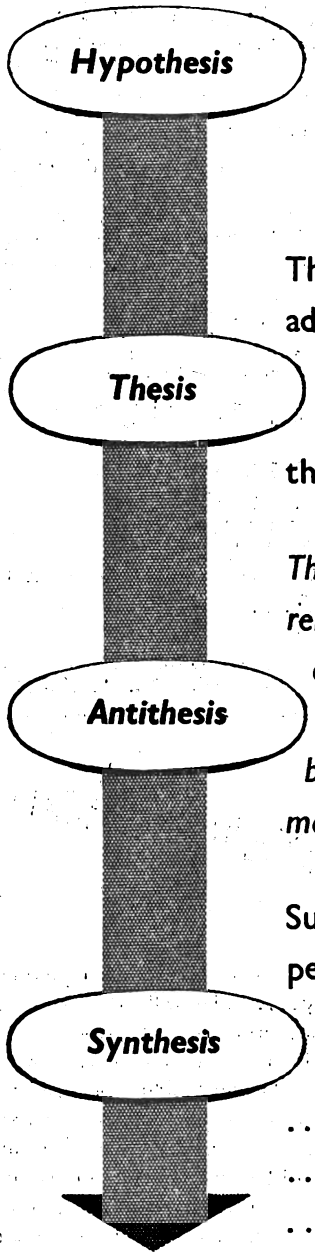
Large-scale diphtheria immunization is telling its own success story . . . . and now the development by Glaxo Laboratories of an efficient whooping cough vaccine brings nearer the promise of a similar trend in the statistical picture of pertussis. For the convenience of *simultaneous* prophylaxis against both these diseases, the pertussis vaccine and diphtheria toxoid have been combined as one immunological weapon. Each cc. of the Combined Prophylactic *Glaxo* contains at least Lf 25 diphtheria prophylactic A.P.T. and 20,000 million H. pertussis (alum-precipitated). The course for primary immunization comprises three injections—0.5 cc., 0.5 cc., and 1.0 cc. at monthly intervals—a feature of clear advantage to those combating these diseases.

GLAXO

DIPHTHERIA–PERTUSSIS PROPHYLACTIC *Glaxo* *In 2.5 cc., 5 cc. and 10 cc. bottles*

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX. BYRon 3434

Digitized by Google



A SULPHONAMIDE SPECIFIC FOR *Pyelitis*

The soluble sulphonamides represent a distinct advance in the treatment of urinary tract infections. Simple to administer, rapid in action and effective against the common causative organisms, they are the agents of choice in such cases.

The excretion products of many of these compounds are relatively insoluble and contain a considerable proportion of inactive acetyl derivatives. Thus the risk of crystallization cannot be disregarded, whilst the systemic blood levels necessary to ensure therapeutic efficacy may produce toxic effects.

Sulphacetamide, by virtue of the following properties, is particularly suitable for and effective in the treatment of urinary tract infections.

... Relatively high solubility in the urine.
... Over 70% excreted as ACTIVE sulphonamide.
... Active against the common causative organisms.
... Low systemic toxicity.

'Albucid' ORAL TABLETS

SULPHACETAMIDE

BRITISH SCHERING LIMITED

167-169 GREAT PORTLAND STREET, LONDON, W.1

258/H

Digitized by Google

THE LANCET

LONDON: SATURDAY, SEPT. 18, 1948

Dietary Fat

THE vociferous demand for a larger fat ration, which has been heard in Germany since the capitulation, has lately been echoed in this country. As Dr. WALKER points out on page 476, BICKNELL believes that our present intake—which is about 60 g. daily—is hopelessly deficient, and Lord WOOLTON regards the deficiency as dangerous. What is the evidence for deficiency? The German claim, which has been voiced insistently by Professor REIN in the Göttingen *Universitätszeitung*, evoked a request for evidence that the very low intake is causing or has caused ill health. None has been forthcoming. Last year German doctors received a printed post-card purporting to give *minimum* dietary fat requirements as laid down by experts. The figures were: 40 g. (Paris, 1941); 100 g. (London, 1945); 20–35% of total calories (U.S.A., 1944); and 80–125 g. (League of Nations, 1938). The Paris reference is to a lecture by Mme RANDOIN,[1] who suggested that animal fat (about 10 g. daily) was required to provide vitamins A and D and part of the vitamin E, and vegetable fat (about 30 g. daily) for the rest of the vitamin E and for unsaturated fatty acids. The reference to London, 1945, was to Starling's *Principles of Human Physiology*, which quotes the British Medical Association report of 1933. This report merely says that "One hundred grams of fat per day is usually accepted as an adequate quantity"—hardly scientific evidence. In 1944 a committee of the United States National Research Council, in defining a "tentative goal toward which to aim in planning practical dietaries," remarked that "There is available little information concerning the human requirement of fat. Fat allowances must be based at present more on food habits than on physiological requirements. . . . It is desirable that fat be included in the diet to the extent of at least 20–25% of the total calories." The statement of the Technical Commission on Nutrition of the League of Nations (1938) reads as follows:

> "The minimum quantity of fat or fatty substances which should be present in the diet is not known. . . . The minimum quantity of fat cannot . . . be established in absolute terms. . . . In countries with a temperate climate . . . the fat intake cannot . . . be very low without leading to under-nutrition since the result is likely to be an inadequate energy intake. . . . Feasible dietary limits might be defined as approximately 80–125 grams of fat for a varied diet of 3000 calories."

It will be seen therefore that the authorities quoted are stating not minimum dietary requirements based on scientific evidence but preferences based largely on guesses.

The craving for fat probably arises for four reasons. First, since fat is absorbed slowly from the gut and slows emptying of the stomach, it has a "satiety value" in delaying hunger between meals. Secondly, food containing fat is easier to eat because of its "lubricating" effect. Thirdly, since fat has more than double the calorie value of other aliments, and since most non-fat foods contain a much higher proportion of water, diets can be less bulky if their fat content is high. (In Germany this may be important for heavy workers but not for normal consumers.) Fourthly, fats are less subject than carbohydrates to fermentation in the gut. At the same time the craving may have an unrecognised physiological origin. Fat can be made from carbohydrate in the body, as many obese people know to their cost. It is not necessary in the diet as a source of the known fat-soluble vitamins, for there is no sound evidence that adult man must have vitamin D for full health, and he gets carotenoids in vegetables, calcium and phosphorus in bread and water, and vitamin E—which he may not need at all—in bread. In young rats, deficiency of essential fatty acids causes cessation of growth, eczema, scaliness of feet and tail, hæmaturia, and death; in dogs eczema develops. There is no proof that unsaturated fatty acids (linoleic, linolenic, and arachidonic) are necessary for health in man, though they probably are. Two different workers have produced eczema in infants kept on diets extremely low in fat; but, on the other hand, BROWN[2] lived for six months on a daily diet containing less than 0·03 g. of fat per kg. of body-weight and observed no ill effects. There is some evidence that a high-fat, low-carbohydrate diet reduces susceptibility to acute respiratory infections, but BROWN showed no increase in susceptibility. Six months in the life of man corresponds to about a week in the rat's life, and rats on the same diet showed signs of deficiency only after a proportionately much longer time; so it is quite possible that if BROWN had continued his diet for longer ill-effects would have been observed.

If we concede that man needs small amounts of certain fatty acids, we still cannot conclude that 60 g. of fat daily is "hopelessly deficient"; bread of high extraction, such as we consume today, probably contains sufficient unsaturated fatty acids to fulfil our physiological requirements. However, if the amount of fat in the diet falls very low, calorie deficiency may result, because the intestine of man is not well adapted to a bulky carbohydrate diet, and this lack of calories may cause famine œdema—which partly explains why fat deficiency is often regarded as an important cause of famine œdema. Cases of famine œdema have lately been divided into two classes[3]: those with low plasma protein so that the diminished colloidal osmotic pressure causes water to pass into the tissues; and those in which the plasma protein is within the normal range and there is probably increased reabsorption of water in the kidney tubules. The great majority of cases seen on the

1. Randoin, L. *Bull. Acad. Méd. Paris*, 1941, **124**, 429.

2. Brown, W. R., Hansen, A. E., Burr, G. O., McQuarrie, I. *J. Nutrit.* 1938, **16**, 511.

3. Sinclair, H. M. *Proc. R. Soc. Med.* 1948, **41**, 541.

Digitized by Google

Continent in the last three years have been of the latter type; and there is no evidence that in these the œdema is caused by fat deficiency.

Provided sufficient calories can be made up from other sources, then, fat in the diet is desirable but probably not essential. Unfortunately, throughout the world foods rich in fats are even scarcer than most other nutritional commodities. This shortage will partly be overcome by the African groundnuts scheme, which might be supplemented by the use of synthetic fats. Research on these was conducted in Germany during the war, and a plant for their commercial production was established at Witten, where fuel was made by the Fischer-Tropsch process from carbon monoxide and steam; a by-product from this process was "gatsch," which consisted of soft paraffins from which edible synthetic fats could be made. These were tested by some distinguished physiologists in Germany, including KARL THOMAS, and were used in feeding the armed forces: the Witten plant could produce some 18,000 tons of synthetic fats annually, from which about 7200 tons of margarine could be produced. Further research should be done on this subject. For the present we must consider ourselves lucky in this country to have a relatively luxurious amount of fat in our diet, and it is not surprising that no scientific evidence has been forthcoming of any harm from shortage. It remains possible that the increased palatability and variety afforded by additional fat would improve the nutrition of our workers and promote production. Of this we know very little and need to know more.

Supplies of Radioactive Isotopes

FEW medical research-workers in this country have yet been able to use radioactive isotopes for tracer studies and there have been no supplies for treatment. Almost all our knowledge of their therapeutic actions and of the application of tracers to medical and physiological problems has so far come from America. But in a statement published on page 469 the Medical Research Council announce that they can now obtain limited quantities of isotopes for approved tracer and therapeutic projects in this country, and regular supplies are expected soon from Canada and later from the British atomic plants, when completed.

The emphasis on tracer research rather than on treatment reflects the American experience, which has on the whole been disappointing in the clinical field. Radiophosphorus (P^{32}), for example, has been extensively tried for the treatment of leukæmias, polycythæmia vera, and Hodgkin's disease; its use is now limited to chronic myeloid leukæmia and polycythæmia. LAWRENCE and his associates,[1] reviewing the results in 129 cases of chronic myeloid leukæmia treated with radiophosphorus, note that only 33 survived five or more years after the onset of symptoms and the average length of life was 3·7 years. These figures are of the same order as those obtained with X-ray treatment, and radiophosphorus therapy is much more difficult to control owing to the ever-present danger of inducing aplastic anæmia and the need for wide variation in dosage in different patients. Polycythæmia patients have survived much longer and had longer remissions; but this accords with the natural history of the disease, and equally good results have been seen with total body irradiation or even with periodic venesection. A new hazard that has appeared with radiophosphorus is that it may induce malignancy or even further leukæmia, though LAWRENCE did not think that the dosage in any of his patients had approached the level at which such lesions were induced in mice, and none of his patients who had survived five years showed any of these changes. The Medical Research Council's suggestion that radiophosphorus should not be given to patients whose expectation of life is over five years seems hardly workable, since at the time of diagnosis there is no way of distinguishing the minority of chronic myeloid leukæmia patients who will survive so long, or of finding out which cases of polycythæmia are of the very slowly progressive type. Opinion on the value of radioactive iodine for hyperthyroidism has not yet crystallised, but there again long survival is surely the aim. It is in the malignant diseases that radioactive isotopes may prove most useful; the council mention radiocobalt, and there is an important field for trial in the use of colloidal gold (Au^{198}) for the localised infiltration of tumours.[2]

Radiophosphorus will cost about 10*s.* and radio-iodine about £1 per millicurie. This means that it will cost £1–2 for the initial course of treatment in chronic myeloid leukæmia, and then from 5*s.* to £1 a week for maintenance. The radio-iodine for a case of hyperthyroidism will cost £40–50 with present ideas of dosage. Under the National Health Service the cost will be a Government concern, but it is nevertheless interesting as one of the factors that can be compared with other treatments giving comparable results. For the treatment of leukæmia, X-ray therapy costs at least as much and nitrogen mustards somewhat less. For hyperthyroidism, thiouracil costs much less; the cost of surgical treatment is difficult to estimate, but when the time in hospital is considered it is probably of the same order as radio-iodine treatment.

No-one should imagine that because a radioactive tracer will help to solve his own particular puzzle he can go straight ahead and count on supplies. Apart from the necessity of obtaining proper apparatus for detecting and handling these materials, two of the council's conditions should be specially noted—that a physicist must collaborate in the research; and that proper safety measures must be taken. The need for a physicist is easy to understand, for the calculations and the apparatus used in this type of work are quite outside the medical field. But how many would-be users of radioactive isotopes realise what is involved in the provision of effective safety measures? To avoid over-exposure of workers, the simplest actions like opening a bottle and filling a pipette have all to be thought out afresh and carried out by remote control so that the worker is protected by suitable screens at every stage. An open beaker containing 5 millicuries of P^{32}, in the form of Na_2HPO_4, radiated 4r per hour 5 inches over the top, 1·2r per hour at contact through the bottom, and 0·06r per hour

1. Lawrence, J. H., Dobson, R. L., Low-Beer, B. V. A., Brown, B. R. *J. Amer. med. Ass.* 1948, **136**, 672.

2. *Lancet*, 1948, **i**, 372.

Digitized by Google

8 inches from the sides. A tenth of a millilitre of a solution of radiostrontium (Sr^{89}) of 125 microcurie activity radiated a tolerance dose (0·1r) in 3 minutes at 6 inches, the normal working distance with a micropipette. TOMPKINS,[3] who gives these figures, shows in a well-illustrated article the minimum requirements for avoiding accidents. As he rightly says, "practice and patience will be required to develop the new manual dexterity and the new ways for conducting laboratory work that are needed." In addition to these complications, special measures have to be taken to avoid contamination of clothing, to control disposal of wastes, and to "monitor" by special devices workers and their instruments for excessive radioactivity. When all this is realised, tracer research is likely to be restricted to the larger institutions which can afford the space and financial outlay for special laboratories in which this work, and this work alone, will be done, with the help of specialists trained to handle these potentially dangerous materials.[4] It is to be hoped that the necessary facilities for using the new supplies will be provided, so that British workers will have their chance to explore the tremendous field of experiment now opened to them.

Health Care

IN their new-found preoccupation with social medicine doctors know well enough that they belong to the social-welfare team; but some are perhaps not so sure of their place on the field or the direction of the goal. The principal cause of this uncertainty is the artificial isolation of one member from another. The evils of this isolation are underlined in a report by Dr. JOHN B. GRANT,[5] who lately undertook for the Rockefeller Foundation a tour of twelve countries in North America, Europe, and Australasia, to assess and compare progress in "health care"—a term to which he gives a wider meaning than medical care. The same pattern is evolving in each country, though in some it is more complete than in others. GRANT divides the evolution of social welfare into three stages. First comes the stage of paternalistic legislation, developed in Britain a century and a half ago, with the aim, based on humanitarian motives, of relieving outstanding ills; all countries have emerged from this stage. The second is the stage of social insurance, intended to provide security for labour by pooling risks; Germany initiated this some sixty years ago and most countries are now in it. The third stage is based squarely on a population policy which aims to improve the quality of human capital by removing social ills.

The funds set aside for social security vary widely from one nation to another. Thus the British social-insurance costs for this year will be at least 10% of the national income; and the South African estimate for 1955 is 15%. On the other hand, in the U.S.A. in 1946 federal expenditure on social welfare constituted only 1·3% of the national income. There is less discrepancy between the nations in their policies for housing and nutrition, which reflect growing concern with population needs. Formerly housing policy was based on rental returns, but, except in North America and Holland, this basis has been superseded by various types of State subsidy to ensure that rentals do not exceed 20% of the wage-earner's income—a limitation which, without outside help, would render the construction of houses for letting uneconomic. Similarly, in the matter of food almost every European country is establishing a policy akin to that in Great Britain, including free or subsidised protective foods, enrichment of certain foods, free school lunches, price control backed by subsidies, and increased production of essential foods.

If medical care is to take its proper place in the changing order, three conditions must be met: removal of economic barriers; provision of sufficient personnel and resources, properly distributed; and technical excellence in medical personnel and equipment. Economic barriers are almost everywhere being brought down; the only two countries where voluntary insurance still receives consideration are the U.S.A and, to some extent, Denmark. In organisation other countries, including the U.S.A., seem likely to follow the regional plan introduced in Britain; and usually such plans are formulated with an eye to achieving eventually 15 hospital beds per 1000 population. The Hospital Council of Greater New York[6] sets the figure at 16·1, which would be divided as follows: general care 4·2 (residents 4·0, non-residents 0·2), convalescent care 1·0, long-term illnesses 2·0, acute infectious diseases 0·1, tuberculosis 0·8, and psychiatric disorders 8·0. GRANT calls for greater initiative outside the hospital; nowhere, he says, is there a health centre fulfilling all the functions envisaged for this institution. The generous provision of hospital beds and of practitioners (1 to 1500 population) which he mentions may not be immediately attainable here. We can, however, take to heart his criticisms of planning in the countries he visited. The most serious is the complete failure, except in Australia, to consider the number and the training of personnel required to work the organisation evoked by legislation. Secondly, except in South Africa, planning and legislation are for sickness rather than health. Thirdly, not enough regard is paid to chronic, mental, and rehabilitative services. Planning, he contends, has gone ahead in watertight compartments; and there is complete disregard of the need for auxiliary personnel. From his survey GRANT concludes that "effective measures for health promotion, disease prevention, and rehabilitation require government action and cannot be attained through voluntary agencies." It is becoming increasingly clear that this is also true of curative medicine.

3. Tompkins, P. C. *Nav. med. Bull., Wash.* March-April, 1948. Supplement on Isotopes and their Medical Aspects, p. 164.
4. Howarth, F. *Lancet*, July 10, p. 51.
5. Grant, J. B. *Amer. J. publ. Hlth*, 1948, 38, 381.
6. Hospital Council of Greater New York. Master Plan for Hospital and Related Facilities in New York City. New York, 1947.

THE INDEX and title-page to Vol. I, 1948, which was completed with THE LANCET of June 26, is published with our present issue. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Digitized by Google

Annotations

THE INDUSTRIAL CONGRESS OPENS

In the early days of the Industrial Revolution machines were more valued than the men who drove them; and it has taken us some time, as Mr. T. E. A. Stowell remarked at the opening session of the International Congress on Industrial Medicine, to realise the importance of conserving the industrial worker. Mr. G. A. Isaacs, Minister of Labour and National Service, mentioned that it is the Government's policy to set up a national industrial health service, coördinated with the National Health Service, as soon as there are enough trained doctors and auxiliary staff to work it. Reviewing some stages in the growth of our industrial medical service, he recalled that Dr. Thomas Legge, the first medical inspector of factories, was appointed just 50 years ago, and was knighted for his success in proposing measures to counteract risks in industry, especially lead poisoning. Other countries have contributed important studies: South Africa, for example, has led in the study of silicosis. For thirty years the Industrial Health Research Board has been issuing important statistics which are ultimately translated into legal requirements and regulations benefiting health. Progress often seems slow; Mr. Isaacs has found it so, he said; but the ground is well prepared, and in the end we get good regulations and enforce them. That the rut of habitual thought may lock the wheel of progress for an unconscionable time, however, was nicely exemplified by Lord Moran's story of a former Minister. Long before the late war the I.H.R.B. had collected figures relating production to hours of work—which were ignored when the pinch came. Yet when Lord Moran handed the harrassed Minister the proof that a man can produce more in 6 days than 7, he only provoked the indignant response: "Don't you know there's a war on?"

But there are more reasons for a falling off in output than unduly long hours of work; and Lord Moran was glad, he said, to see the changing conception of industrial medicine. Nowadays it is concerned not merely with the physical hazards of industry but with the mental and emotional hazards as well—with the proper study of mankind, in short. What makes a man stick to his job? "Work or want" has fortunately gone, in this country and for this time, as an incentive. What takes its place? What industrial medical officer, he asked, is going to write an *Anatomy of Contentment*? If a man is contented his production is high, and efficient production means social security. As Dr. Lloyd Davies urges on p. 465, we must no longer think of work in terms of whether it is harmful but whether it is beneficial to free men with unfettered minds. The secret of a contented mind may be to do a job well.

A PIPERAZINE ANTHELMINTIC

To the growing list of anthelmintics has now been added a piperazine derivative. Formerly the piperazines were administered as urate solvents, and their reintroduction follows the observation that some derivatives were effective against the filarial parasite of the cotton-rat. Of more than 1000 compounds tested by the Lederle Laboratories the one which was most effective and least toxic was 1-diethylcarbamyl-4-methylpiperazine, known more briefly as 'Hetrazan' diethylcarbamazine.

Extensive trials of hetrazan have confirmed that, with a few hundred milligrammes by mouth in divided doses over a period of 3–7 days, *Wuchereria bancrofti* quickly disappears from the blood-stream. It usually reappears a few days after the drug is discontinued; but in patients receiving similar courses lasting altogether 3–4 weeks the parasite has sometimes remained absent for about a year. From the U.S.A. have come reports suggesting that the drug may cure bancrofti infections by killing the adult worm. In any event, the administration of hetrazan for short periods is so effective in freeing the peripheral blood of microfilariæ as to suggest the possibility of breaking the filarial cycle at the link between man and mosquito, for man is the only known host. Against other filarial infections of man this preparation seems to be less effective; but trials are not yet complete. As often happens with new drugs, there has been some trouble with toxicity. Patients receiving hetrazan are not confined to bed; and their chief complaints have been of headache, lassitude, and vague malaise. These symptoms come on within a few hours of the treatment being started, but usually disappear within 48 hours, even where administration is continued. The compound seems to be stable under a variety of climatic conditions.

STREPTOMYCIN IN NON-TUBERCULOUS INFECTIONS

The serious toxic effects common in the cases of meningeal or other forms of tuberculosis treated with long courses of streptomycin need not deter the clinician from using the drug for short periods in other infections. But at this stage, when information concerning dosage and indications is badly needed and supplies are relatively short, it is in everyone's best interest that suitable cases should be treated in hospitals which are fully equipped with laboratory facilities, so that both diagnosis and treatment can be bacteriologically controlled. On another page Prof. Clifford Wilson summarises the main findings of the Streptomycin Clinical Trials (Non-tuberculous Conditions) Committee. The treatment of many of the conditions mentioned is still in the experimental stage, and it seems advisable to confine the use of streptomycin to the treatment of meningitis and septicæmia due to gram-negative bacilli and other penicillin-resistant organisms which have been found to be streptomycin-sensitive. We understand that a small amount of streptomycin may be available for distribution in the regions for the treatment of these conditions.

POSTURE IN ANÆSTHESIA

Man's complex respiratory and circulatory mechanisms are adapted to the erect posture. They depend on a series of reflexes involving the voluntary muscles, often affecting muscle tone. In the operating-theatre, the patient is placed in one or other of several unnatural postures. Some of the effects of these postures are unavoidable. Others, equally distressing, follow improper supervision of placement on the operating-table. Three anæsthetists have lately underlined the effects of such unnatural postures. From observation on experimental animals and on man Gordh [1] confirms that deep anæsthesia abolishes most, if not all, of the compensatory mechanisms involving vasomotor tone which are normally brought into play by change of posture. He emphasises the value, as a resuscitative measure, of a head-down tilt—to us the familiar Trendelenburg position. The increased venous return in this position ensures good filling of the right heart, which results, in accordance with Starling's law, in slowing of the pulse-rate and rise in the blood-pressure. In animals the head-down position acts as an effective cardiac stimulant even after a few minutes of cardiac arrest.

Hasler [2] draws attention to the reduction in the vital capacity so common in the anæsthetised patient. This is remedied by a moderate head-down tilt; but when the tilt is excessive the effects are far from good. The extreme Trendelenburg position, so beloved of the

1. Gordh, T. *Acta chir. scand.* 1945, suppl. 102.
2. Hasler, J. K. *Proc. R. Soc. Med.* 1948, **41**, 133.

Digitized by Google

gynæcologist, draws the abdominal contents away from the pelvis but deposits them on the diaphragm, so respiration may be seriously hampered. With a tilt of 30° the vital capacity is reduced by some 15% and some basal pulmonary atelectasis seems to be the rule. The head-down tilt is not alone in producing this evil effect; the gall-bladder bridge, the lithotomy position, and even the lateral kidney position all reduce the vital capacity by similar amounts. None of these can be exonerated as causes of postoperative "chests."

Among the more preventable ill effects are those due to malposition of the patient.[3] Here the harm is done by pressure on certain structures, notably vessels and nerves. Even the junior student knows that the arm hanging over the edge of the table is likely to cause a "Saturday-night palsy." Less familiar are the brachial-plexus palsy due to malplaced shoulder-rests, pulmonary embolism due to pressure on the calves, and damage to the eyes due to trauma during operations on the head and face. These complications are avoidable by constant vigilance on the part of all in the operating-theatre. Nurses have long been taught that an anæsthetised patient gives no warning that his water-bottle is too hot: in the same way students should learn that a patient who makes no response to the deliberate trauma of the operation also does not respond to any other trauma.

HOSPITAL BUILDING

MUCH of the hospital accommodation in Great Britain is obsolete or obsolescent, and the need for extensive capital expenditure was one of the most obvious lessons of the surveys undertaken by the Ministry of Health during the war. It was therefore one of the underlying factors which tilted the scales in favour of nationalisation of the hospitals. The principles now being laid down by the Minister for the guidance of regional boards and governors of teaching hospitals in their building projects are therefore important. In general, the Minister is willing to leave projects costing less than £10,000 to their discretion, but he retains, of course, the responsibility for settling priorities as between the various schemes submitted, since the total cost of labour and materials must not exceed the total allocated to the Ministry for hospital purposes and the whole cost will have to be borne on the Ministry's estimates. In present circumstances, moreover, all schemes costing more than £100 must first be authorised by the Minister under regulations which apply to any kind of building in this country.

The allocation of priorities thus vested in the Minister will be no enviable task. There are a great many small schemes of adaptation and improvements which must go forward. Clearly such objects as nurses' accommodation and improvement of catering facilities must receive high priority. Even if no new wave of hospital construction can take place for some time, the central department in Whitehall will need to become thoroughly expert on many subjects affecting hospital accommodation. In the United States the Public Health Service has in the last few years built up an extensive section for the approval of plans submitted under the Hill Burton Act and is sponsoring expenditure running to some 70 million dollars a year. Their relations with the hospitals are most cordial and it is much to be hoped that our own Ministry will send its officials out far and wide into the hospital world, so as to obviate the danger of decisions being taken solely on rules and regulations. In the past, the necessity to raise the funds for proposed alterations has been some safeguard against unessential schemes—not always a very satisfactory test, since it also excluded many much-needed improvements in the poorer localities. The new system with Government money behind it will work better than the old only if flexibility and continuous personal contact are assured. It would be no bad thing if every officer in Whitehall concerned with hospital administration spent a month each year in travelling round the hospitals with no particular agenda, to learn at first hand how the current rules and regulations tend to hamper the individual hospital.

3. Slocum, H. C., O'Neal, K. C., Allen, C. R. *Surg. Gynec. Obstet.* 1948, 86, 729.

STUDENT NURSES' SALARIES

THE arguments in favour of raising the training allowance of student nurses were strong when stated in these columns by a correspondent eighteen months ago,[1] and they have since grown stronger.[2] When so much depends on finding and keeping enough new entrants to nursing, it is important to be able to assure the possible recruit that during training she will need no financial support from home—support which many parents of suitable girls are not in a position to provide. Much has of course already been done to improve the lot of the student nurse, and in outlining its many advantages Dr. MacWilliam [3] rightly points out that there is a limit to what an impoverished country can offer for the services of a novice of 18. Nevertheless we are glad to learn that the Nurses and Midwives Whitley Council, meeting on Sept. 13, has in effect agreed to our correspondent's recommendation of a cash allowance of £100 a year. Under the new arrangements students entering training after Jan. 1 will receive £200 a year, out of which those resident in hospital will have to pay £100 for board and lodging—as well as income-tax and National Insurance and superannuation contributions. Existing first-year students, and those recruited before the end of the year, will, if resident, receive £100 a year, and free residential emoluments. Those who live out will receive free meals on duty, uniform, and laundry, besides their training allowances, and in future there will be dependants' allowances of 10*s*. a week for an adult and 5*s*. for the first child. Slightly higher training allowances will be paid to second-year and third-year students, who carry more responsibility, and to students in the special fields of tuberculosis nursing and midwifery. The basic £200 for the first-year student in general training may be compared with the present salary of £145 (for a woman) of which £70 is paid in cash and £75 represents the value of residential emoluments. (Before July 5 the three figures were £130, £55, and £75.) In future the training allowances will be the same for men and women.

The remuneration of student mental nurses and of student nursery nurses is still under consideration.

LEGITIMACY AND ARTIFICIAL INSEMINATION

ITEMS of news about artificial insemination always attract keen popular interest. The *News of the World*, in its issue of Sept. 5, published a report from its New York correspondent concerning the legitimacy of what we are learning to call a "test-tube baby." A wife, it is said, asserted that her husband "on her wedding night in New York informed her that he was unable to become a father and suggested that she consent to artificial insemination." She did so and a child was born. Apparently husband and wife afterwards parted company, for there were legal proceedings in a New York State court over the custody of the child. The judge awarded "principal custody" to the mother but allowed her husband the right of occasionally visiting the child. The wife asked for a declaration that the child was illegitimate, presumably in order to exclude the husband's right of making visits. The New York judge refused. Such a decision, he observed, would be "inhuman, inhumane, and contrary to the highest

1. *Lancet*, 1947, 1, 190.
2. *Ibid*, Aug. 7, p. 225.
3. *Ibid*, Aug. 21, p. 313.

Digitized by Google

concepts of sociology." He declared the child to be legitimate and the husband to be the legal father. Apparently he laid stress on the fact that the artificial insemination took place with the husband's knowledge and consent. The wife then moved into another State's jurisdiction and obtained from a court in Oklahoma City a ruling that she was entitled to the complete custody of the child.

Into the consequences of a conflict of laws as between different State jurisdictions in the U.S.A. we need not enter. The Oklahoma decision was perhaps a question of custody rather than of legitimacy. The action of a wife in seeking to bastardise her own child is unusual and not such as courts would normally encourage; the material evidence would be of a nature which in some jurisdictions is excluded. Be that as it may, the vital distinction, not clearly drawn in the necessarily abbreviated report to which we have referred, is whether the donor of semen is the husband or someone else. The two eminent legal authorities who contributed to the report of the Archbishop of Canterbury's Commission on Artificial Human Insemination [1] held that, if the donor is not the husband, the child is illegitimate; the fact that the husband has consented to the operation does not affect the position.

THE HEALTH CENTRE

IN the spring of last year the British Medical Association set up a committee, with Dr. Talbot Rogers as chairman, "to investigate and report on existing forms of group practice, including partnerships and other forms of collaboration between general practitioners and to relate this and other experience to health centre development." As part of its task the committee arranged a field survey of present-day practice, and the first part of the B.M.A. council's interim report [2] on the subject is devoted to an analysis of this survey. The conditions under which the general practitioner works are described and an analysis is attempted of the advantages and disadvantages offered to patient and doctor by differing methods of practice. Singlehanded practice is contrasted with various forms of partnership, or group practice, and while agreeing that "there are many highly efficient and successful practitioners working singlehanded, and some who could not work satisfactorily in any other way . . . the council considers the advantages of partnership practice outweigh its disadvantages; it is difficult to conceive a type of general practice more suited to the needs of the present day than a partnership of doctors combining the fine traditions of the family doctor with a variety of interests and experience."

The council emphasises the need for retaining in any future general-practitioner service those features of past methods of practice which have been "largely responsible for the high standard of medical work in Great Britain." Among these it counts the personal doctor-patient relationship, the intellectual stimulus of working in contact with colleagues from a common place of work, the variability and flexibility of practice to suit different conditions, the voluntary nature of partnerships, and the freedom of doctors to organise their work as they think best.

Equal care is taken to detect present defects needing to be remedied in future practice. Chief among these is placed the divorce of preventive and therapeutic medicine, which has ensued with the development and multiplication of local-authority clinics. Throughout the report the necessity is urged for the re-association of these unwisely separated compartments of medical practice so that the practitioner and the public-health officer may coöperate, and sharing each others' tasks be better able to give a continuous and coördinated service to the families under their care. Unnecessary isolation of doctors should be ended; better and more labour-saving professional premises should be available; and ancillary, secretarial, nursing, and dispensing help should be put to the greatest possible profitable use. Hospital beds should be provided in which general practitioners could continue to care for patients who need nursing help but not necessarily specialist investigation and treatment. Special emphasis is placed upon the need for easy access by general practitioners to diagnostic facilities, particularly in the fields of radiology and pathology. From these considerations the council comes inevitably to the conception of the health centre—"a well-equipped building housing a group of doctors who carry out in a coördinated way all the work at present done by general practitioners and clinic medical officers." The range of service to be provided in such a centre is suggested, and methods of staffing and administration are discussed. The council has not given its final answer on all arguable points—some it has reserved for further discussion. Perhaps the one upon which we shall most urgently await the council's opinion in its promised final report is that of the need for the provision in health centres of specialist services (including particularly radiological and pathological facilities). Meanwhile enough agreement has been reached for the council to be able to suggest that in urban areas a health centre should be the headquarters of up to eight practitioners serving a population of about 25,000, and to summarise the type and extent of the accommodation that would be needed to provide services adequate to such a population. This detail of accommodation should be just what the architect needs as the foundation for his planning, and it is to be expected and hoped that the publication of the council's report will be a stimulus to the production of a variety of plans suitable for health-centre construction.

But this alone would not satisfy the council, who rightly stress the urgent need for actual experimentation in health centres. Regretting the conditions which necessitated the issue of circular 3/48, which discouraged local authorities from submitting immediate proposals for health centre provision, the report goes on to say that "there are new towns and large housing estates being constructed in which some kind of accommodation for the health services will have to be built; in these it would seem an actual economy to build health centres in the most convenient sites, instead of separate premises for the doctor's surgeries and the local authority services." The council in conclusion reports that it "is satisfied that the most satisfactory form of practice at present and in the immediate future is partnership practice from a common surgery. It believes that the logical future development will be the provision of specially designed health centres from which both general practitioners and the present local authority services can be provided. . . . Early experiment is advisable and a central committee should be established without delay to offer guidance during this experimental period and to collect information of the results achieved."

This report last week had a favourable reception in the national press. It was described as a document of great value, and we may well concur, for the council has done a great constructive service, first by its careful field survey, and secondly by its clarification of the problems involved and its suggestions for their wisest solution. The report should become a landmark in the story of health-centre development, and we hope that it may prove of great assistance to the members of local authorities, of executive councils, and of local medical committees, in whose hands the future of health centres now lies, and upon whose enthusiasm their early development will depend.

1. See annotation, *Lancet*, Aug. 21, p. 298.
2. *Brit. med. J.* Sept. 11, suppl. p. 107.

Digitized by Google

Special Articles

THE MORALS OF EMPLOYMENT*

T. A. LLOYD DAVIES
M.D. Lond., M.R.C.P.
CHIEF MEDICAL OFFICER, BOOTS PURE DRUG CO. LTD., NOTTINGHAM

"I CAN'T do it, doctor. Every time I goes on the job—it's me stomach, doctor." This is the problem which constantly faces industrial medical officers. An apparently healthy and normal person, working in healthy, good, or even the best possible working conditions, finds the work repulsive. Is such a patient to be forced to undertake work under those conditions because the vast majority of his fellow workers find those conditions satisfactory or even to their liking? Or is he, because he makes complaints which, though genuine, cannot be substantiated by any subjective or objective test, to be allowed to change the conditions of his work? This is not a medical problem; it is a moral problem and one that, however hard we may try, we cannot avoid.

In these times, which politicians and more reliable judges of mankind have foreseen will be known as the age of the Common Man, it is paradoxical that the personal relationships of the Common Man have been lost in the masses. A workman is engaged by an employer to do so much work, under certain conditions, for so many hours, for a certain amount of money. Perhaps, when trade unions meet employers, these items are the only matters which can be clearly defined, but the essence of a contract of employment is not the quantity of work or the rate of payment but trust and mutual welfare.

Suppose my patient is a bus-conductor. He is engaged by a bus company to issue tickets to passengers for so many hours a day, with so many hours stand-over and so many hours turn-round time. He is provided with canteens at terminals, and he is paid wages which have been agreed between his employer and his union. A few bus-conductors may be promoted to inspectors, but for the vast majority there is no relation between their interest in their work, their enthusiasm, the amount of work they do, or their politeness to passengers, and their rewards, whether these be in working conditions, hours of work, or wages. To me it would be dreadful to know that I was committed for the rest of my life to earn wages which are predetermined, prejudged, and unalterable, whether I did my best to further my employer's interest, or whether I merely took care not to get the sack.

Rewards of work are many: first, wages; secondly, the power that wages bring; and thirdly, the opportunity of "malice, hatred, and all uncharitableness." But the only true reward of work is that it provides satisfaction to the body, mind, and soul. Alas, work has become synonymous with employment, divorced from the zest and pride of a good job well done. Individuality has become lost in agreements between unions and employers, so that the clock, with inexorable precision, signals when the unceasing burden of employment shall subordinate the thought, fancy, and action of my patient to those of his neighbours. Let anyone who doubts this look at the appalling disgorgement from the mills and factories, at the end of the day, of hurrying discordant human beings (in the modern jargon, personnel). Lest one moment should be their own, they anxiously run to amusements and time-wasting sports where the gregarious instinct denies an appreciation of the real purpose of living.

"Economic necessity" is said to be the reason for asking married women to return to the mills and factories at a time when the hours of men are being shortened. Was self-deception ever more blatant? For "economic necessity" is only a term which enables our own laziness to be blamed on a vague impersonal theory. Women must work for mammon instead of for their children.

The break-up of homes and families will extract a high price from the future. Benevolent authority, efficient school-teachers, balanced school meals, national milk, and orange-juice are poor substitutes for the worst parents. Both at home and at work the art of living is sacrificed to the spurious efficiency of material comfort. The idea of religion is even more unfashionable than the word. Instead of feeding boys and girls on algebraic equations and free milk, schools would do better to teach the inadequacy of man.

In the past we have discussed how many accidents take place at work, whether there is a toxic risk, or whether there is risk of harm to the workman, but this is not enough. If we are to build a country worthy of mankind we must think of work in terms of a job, freely entered, freely done, giving physical well-being, mental exercise, and spiritual hope.

* * *

Such a revolution in the conduct of human affairs is not a vague expression of humanistic hopes but a practical aim capable of immediate realisation. Craftsmanship is neither possible for, nor within the abilities of, all, but pride of achievement is still within the reach of those who seek fulfilment in living. The attitude of mind to work is as important as the job; to make certain that work gives the opportunity of interest and joy is the function of management; to seize that opportunity is the chance of the individual. The revolution of human beings, or the demechanisation (from within and from without) of the human body and soul, would achieve more for human well-being and happiness than all the material advances of the Industrial Revolution.

We must no longer think of work in terms of whether it is harmful but whether it is beneficial to free men with unfettered minds. When next, as employers, doctors, and workmen, we interview my patient who finds his work distasteful, let us remember that perhaps, unlike his fellow men who have become conditioned to disharmony, he has kept alive the spark of divine grace, so that before he can attain fulfilment he must have satisfaction in his work. He, not they, more nearly approaches the normality intended for mankind.

* Based on a paper read at Roffey Park Rehabilitation Centre training course in April, 1948.

PROPRIETARY MEDICINES UNDER THE NATIONAL HEALTH SERVICE ACT

E. W. GODDING
CHAIRMAN, STANDARDS COMMITTEE, CHEMISTS FEDERATION

IT is clearly essential that the best medicines should be freely obtainable in a comprehensive National Health Service. But under National Health Insurance economy in prescribing was fostered by the substitution of drugs and by other questionable methods which often discouraged the conscientious doctor, and were responsible, at least in part, for "the panel" being regarded by the public as a second-rate service.

Hitherto, many new remedies have been produced as the result of research carried out by private firms, and if the N.H.I. policy of discouraging the use of proprietary medicines is adopted in the National Health Service the stimulus for research work by the pharmaceutical industry will be destroyed. Further, if the industry is discouraged from a vigorous policy of development the way may eventually be opened for an influx of foreign proprietary medicines. Active discouragement of proprietary medicines may therefore have long-term adverse effects on our national economy.

PRESCRIPTION OF PROPRIETARY MEDICINES

To determine how far the N.H.I. machinery discouraged conscientious prescribing, some retail pharmacists were invited to carry out surveys of about equal numbers

Digitized by Google

of N.H.I. and private prescriptions covering the same districts and the same period. The results, showing the ratios of proprietary medicines appearing in each group of prescriptions were as follows:

	N.H.I.	Private
LONDON S.W. AREA (MAY, 1947)		
No. of prescriptions	1422	825
Proprietary medicines prescribed	82 (5·8%)	165 (20%)
LEICESTER CITY AREA (MAY, 1947)		
No. of prescriptions	755	1000
Proprietary medicines prescribed	70 (9·3%)	398 (39·8%)
GLASGOW CITY AREAS (JUNE, 1947)		
No. of prescriptions	653	1003
Proprietary medicines prescribed	23 (3·5%)	347 (34·7%)

To obtain further information on this question, with the coöperation of certain pharmaceutical houses, 118 doctors were sent an explanatory statement and an invitation to sign the following letter:

Dear Sirs,—In reply to your letter I would confirm that, in my opinion, the machinery for the control of excessive prescribing, under the present National Health Insurance Act, also operates to discourage and dissuade the practitioner from prescribing many proprietary medicines which he considers useful for the treatment of his private patients.

Of the 118 doctors approached, 64 signed this letter; one signatory was the chairman of a panel committee. Since no steps were taken to ensure that the doctors concerned were a representative sample of the medical population, and since the reasons for not signing the letters (many doctors were on holiday) are not known, no statistical significance can be attached to the results. From the readiness with which the letters were signed, however, there is little doubt that a very large number of signatures could have been obtained.

Taken together the results of these two inquiries suggest that, where doctors are free to prescribe what they consider best for their patients, a much higher proportion of proprietary medicines is used, and it seems reasonable to infer that practitioners have not felt free to follow their judgment in prescribing for their N.H.I. patients.

On the other hand, though documentary evidence is not easily obtained, verbal reports of excessive prescribing under N.H.I. have often been received from pharmacists. As an example, when a N.H.I. patient left a district his landlady approached a pharmacist to dispose of 37 bottles of liniment, all unopened, prescribed for him by a local doctor. It does not require many such instances to show that the elimination of wasteful prescribing would pay for many useful proprietary medicines.

The following principle is offered as a basis for the prescribing of proprietary medicines in the National Health Service:

Any proprietary medicine showing a significant therapeutic advantage over existing B.P. preparations can be prescribed under its proprietary designation.

The interpretation of "significant therapeutic advantage" obviously requires expert opinion. It should be noted that the term applies not only to new compounds but also to improved methods of presentation, providing these have a therapeutic significance. For example, though two preparations contain the same active ingredient, in one the drug may be presented in such a way as to act more quickly than in the other. Again, the potency of a drug may be maintained through the use of stabilising agents; and where particularly nauseating drugs are concerned special flavourings may also offer therapeutic advantages.

The practitioner should be given the duty of applying the criterion "significant therapeutic advantage," thus placing the initial responsibility where it rightly belongs. Any alternative system of central or local control must undermine the basis of professional practice. At the same time, routine checks of unnecessary prescribing should be made locally and centrally along the lines in force under the N.H.I.

It is suggested that scientific, medical, and pharmaceutical representatives, with scientific members of the pharmaceutical industry, should serve on a central advisory technical committee whose main function would be to provide the Minister of Health, when necessary, with an expert interpretation of the criterion "significant therapeutic advantage." Reference to such a committee would be preferable to the too rigid control which would be imposed by adhering to an approved list of proprietary medicines, and it should avoid the anomalies which would almost certainly appear if local committees were to act independently. A further advantage would be the avoidance of the delay which would inevitably occur in admitting new products to an approved list of proprietary medicines.

The function of local medical committees as regards the prescribing of proprietary medicines would be to recommend, as was the duty of the local panel committees, what surcharges, if any, should be made in cases referred to them by the central authority.

COMMENTS

The effect of the suggested system, so far as the pharmaceutical industry is concerned, would be to ensure financial rewards for research and development work until the resulting new preparations were absorbed into the *B.P.* Doubt has, however, been expressed as to whether such uncertain rewards would ensure the continued application of the industry's resources in the development and presentation of the new therapeutic substances. More definite incentives might therefore be considered. It is true that patent rights provide, on occasion, considerable financial rewards, but this method cannot be universally applied. Some protection for manufacturers' trade names might be considered, and in this connexion it is worth noting that in many hospitals and Government departments scant respect is at present paid to the registered names of manufacturers' proprietary preparations.

It is only fair to add that a recent Ministry of Health leaflet [1] states that "there will be no restriction on the drugs which may be ordered for free supply for the proper treatment of any patient so long as they are medically necessary." Further, the Minister of Health said in the House on June 24 that patients are entitled, under the new health service, without restriction, to every kind of drug and appliance necessary for their treatment. He added that any doctor who failed to prescribe these drugs would be breaking his terms of service.

The provisions [2] under the new Act for the surcharging of any doctor who is judged guilty of excessive prescribing, which are very similar to those which applied under N.H.I., have not yet been used for the enforcement of restrictions.

The prescribing of proprietary medicines in the National Health Service will clearly require further official consideration, but given a sense of responsibility by all concerned it should not be difficult to find a satisfactory answer to this question. As in all Government organisations, it is essential to avoid the sacrifice of creative ability and enterprise and to preserve a high level of conscientious service.

CONCLUSION

The Ministry of Health has a new responsibility towards the pharmaceutical industry. Until now the substantial part of the population outside the scope of

1. General Medical Services. Arrangements Affecting the General Practitioner. April, 1948.
2. Statutory Instruments 1948, no. 507.

Digitized by Google

National Health Insurance has made it possible for the industry to follow a vigorous programme of research and development, but this position may be sharply reversed if the policy under N.H.I. is continued and extended in the new service.

To accept the benefits of the industry's research while denying it the material encouragement for continuation must have a disastrous effect on its future; on the other hand, the stimulation of further research and development by the industry would contribute much to a vital and progressive health service.

I have received invaluable help from Mr. L. Boon of Genatosan Ltd., and Mr. W. W. Knott of Parke Davis & Co. Ltd., in obtaining the data quoted in this article.

INTERNATIONAL ORTHOPÆDIC CONGRESS IN QUEBEC

A COMBINED meeting of the American, British, and Canadian Orthopædic Associations was held in Quebec from June 3 to 6, under the joint chairmanship of the presidents of the three associations: Dr. R. I. HARRIS of Toronto (A.O.A.), Mr. S. ALAN S. MALKIN (B.O.A.), and Dr. EDOUARD SAMSON (C.O.A.)

SLIPPING OF THE UPPER FEMORAL EPIPHYSIS

Dr. S. KLEINBERG (U.S.A.) maintained that incipient slipping of the upper femoral epiphysis called for elimination of the epiphyseal plate by drilling and the postponement of weight-bearing till there was clear evidence of epiphyseal fusion.

Dr. BECKETT HOWORTH (U.S.A.) reviewed 254 cases, of which 224 had been treated surgically. Operations had included attempted manipulative reduction (37), open reduction (35), transcervical osteotomy (7), subtrochanteric osteotomy (10), and insertion of a bone peg in the front of the head (134). In 131 of the last group, healing occurred without further trouble. The condition should be treated at the earliest stage, when pegging was the procedure of choice; drilling without pegging was ineffective. He advocated early movement. Closed reduction was only possible if slipping had been recent.

Dr. CLARENCE H. HEYMAN (U.S.A.) had followed 42 cases for 2 years and found a good result in 30. Manipulation had given a good radiological and excellent clinical result in 17, and a good radiological result in a further 14. The results in the 8 cases of surgical osteotomy were poor, with aseptic necrosis in 7. Cheilotomy of the anterosuperior part of the femoral head in 3 cases gave much-improved function without degenerative changes. In 8 patients submitted to 10 operations for surgical fusion of the epiphysis clinical and radiological results were good.

Dr. PHILIP WILSON (U.S.A.) dismissed the possibility of an endocrine cause, preferring to think it mechanical, as was the treatment. Early diagnosis, with nail fixation, was important. He believed that cases thought to have done well with manipulation would have done equally well without it.

DEVELOPMENTAL COXA VARA

Dr. A. B. LEMESURIER (Canada) reviewed developmental coxa vara, which, he said, usually first became evident with a limp or waddle at the age of 3–4 years. Familial cases occurred. The most characteristic feature was a gap in the bony femoral neck, which usually filled eventually. Intertrochanteric osteotomy had been performed in 12 cases, and in all but 1 the gap had been speedily closed. A case seen before important coxa vara had developed might be treated by a central bone-graft.

Dr. WILLIAM T. GREEN (U.S.A.) regarded the condition as a failure of ossification of a part of the femoral anlage. In order to secure sufficient abduction, intertrochanteric osteotomy was preceded by adductor myotomy.

Dr. ALBERT KEY (U.S.A.) considered that disappearance of the gap, which did not always happen spontaneously, might be accelerated by drilling. In adult cases he had chiselled away the great trochanter without much further weakening of the abductors. A Whitman's reconstruction had been followed by osteo-arthritis of the new joint 15 years later.

ARTHROPLASTY OF THE HIP

Dr. ALEXANDER GIBSON (Canada) reviewed 104 cases of vitallium-cup arthroplasty of the hip with the Kocher posterior approach. The results were: good, 55; satisfactory, 21; poor, 14; unclassified, 14.

Dr. PAUL C. COLONNA (U.S.A.) thought that it would be difficult to deal adequately with contracted soft tissues, particularly the ligament of Bigelow, through a posterior approach, and that weight-bearing at 4 weeks, as practised by Dr. Gibson, was unusually early.

Dr. M. N. SMITH-PETERSEN (U.S.A.) had always aimed at producing congruous surfaces, and it was to secure adequate exposure of the acetabulum that his approach had been developed.

CONGENITAL DISLOCATION OF THE HIP

Dr. JUAN A. FARILL (Mexico) spoke of operation on cases of irreducible congenital dislocation of the hip without gross deformity of the femoral head or acetabulum. A wide exposure of the hip was supplemented by subtrochanteric femoral shortening and by the formation of an extra-articular shelf if the acetabulum was shallow. Reduction had been secured in all of 12 cases and had been maintained in 11. No necrosis of the femoral head had been observed.

ARTHRODESIS OF THE ANKLE

Dr. W. E. GALLIE (Canada) described arthrodesis of the ankle-joint by a method which he had used in 25 cases without failure. Near each margin of the joint an anteroposterior mortice was cut, half in tibia and half in talus, each channel being about $1^1/_4$–$1^1/_2$ in. high and about $^1/_2$ in. broad. A tibial graft was then driven into each of the mortices. The articular cartilage was not removed.

COMPRESSION ARTHRODESIS OF KNEE

Mr. JOHN CHARNLEY had followed Dr. Albert Key in arthrodesis of the knee by pin fixation of each fragment and bracing the pins together in such a way that they could be forcibly approximated so as to impact the cut bony surfaces with a force of the order of 50 pounds. In 17 consecutive cases of osteo-arthritis (degenerative arthritis) or healed tuberculous arthritis, the junction had been solid by the 21st, 14th, and even 12th day after operation.

ARTHROPLASTY OF THE KNEE

Dr. HAROLD B. BOYD (U.S.A.) for Dr. J. S. SPEED and Dr. PHILIP C. TROUT had followed up 64 cases of fascial arthroplasty of the knee for 5–25 years or longer. It took 5 years to achieve full improvement, and thereafter function remained surprisingly constant. Only cases following acute infective arthritis or trauma were selected. The operative technique was that of Campbell. The results were as follows: good, 28; fair, 17; poor, 8; failures, 11. The poor results were due to inadequate movement (4), instability (1), both inadequate movement and instability (2), pain in addition (1). The authors concluded that: (*a*) careful selection was imperative; (*b*) granted this, 70% of patients should have good or fair results, and another 12% would prefer their final state to that of ankylosis; (*c*) major functional adaptations might occupy 5 years; (*d*) if instability appeared, it usually did so during this period; (*e*) thereafter the condition was usually maintained over many years; (*f*) recent advances, notably the development of penicillin, had greatly diminished the number of suitable cases requiring arthroplasty.

Dr. J. EDOUARD SAMSON (Canada) reviewed the results of 50 operations for arthroplasty of the knee in 43 patients, all over 20 years of age. He adopted a simple technique embodying sufficiently wide resection; the preservation of an intercondylar tongue of tibia, the lateral ligaments, and the patella; and the interposition of a free flap of fascia lata. 'Cellophane' had been used in 2 or 3 cases, but had caused a reaction and needed removal. Except in a few of the earlier cases, no physiotherapy was given, beyond active exercises, but nearly all received 1–4 conservative manipulations. The functional results were always better than the radiological, and were classified as follows: excellent (painless, stable, with flexion to 90°) 15; good (similar, but with flexion to 40–60°) 14; fair (similar, but with flexion to 20–40°) 9; bad 15, including re-ankylosis 12 (with infec-

Digitized by Google

tion 4), instability 1, and pain 2. Dr. Samson concluded that (*a*) arthroplasty of the knee had a place in major surgery, (*b*) it carried no inordinate risk, (*c*) gonorrhœa had, till now, provided the most frequent and most favourable cases, (*d*) cases of rheumatoid polyarthritis should not be operated upon unless arrested; (*e*) cases due to osteomyelitis or tuberculosis were unsuitable; (*f*) good musculature was imperative, and (*g*) the patient's coöperation was indispensable.

DENERVATION OF THE ELBOW-JOINT

Dr. JAMES E. BATEMAN (Canada) had performed neurectomy for the relief of pain in the elbow-joint on 150 cases. The operation was carried out through three incisions—at the medial border of biceps tendon, at the lateral border of biceps tendon, and posteriorly for the nerve to anconeus. Of 8 patients followed up after neurectomy for pain from osteo-arthritis or traumatic arthritis, all had less pain and showed a slight increase in the range of movement.

SUBTROCHANTERIC LIMB SHORTENING

Dr. LAWSON THORNTON (U.S.A.) described a method making use of the nail-plate designed for the treatment of intratrochanteric fractures. The nail was driven into the neck of the femur, and then the appropriate length of femoral shaft was excised immediately below the great trochanter; a spur was left attached to the inner part of the upper fragment, to control rotation. The fragments were brought together and fixed by means of screws and the nail-plate.

MENISCI OF THE KNEE

Mr. I. S. SMILLIE reported that 1300 menisci removed in 7 years included 28 which he considered discoid. He classified them as "primitive" (15), approximating to complete discs; "intermediate" (7), less clearly discoid; and "infantile" (6), being broad menisci with a very thin central zone and somewhat resembling the meniscus of the full-time fœtus. Of the menisci, 8 showed cystic degeneration—a change found in 22% of 468 lateral menisci excised. The other lesions found in the discoid menisci varied with the anatomical type. Only 4 of the primitive discs caused snapping; the others were found in the course of meniscectomy for other symptoms. Besides producing a depression in the upper surface of the meniscus, the femoral condyle exerted a grinding force upon the meniscus and so produced horizontal cleavage. The consequent rift tended to open secondarily on to the lower surface and later the upper, but the horizontal character of the main defect could still be demonstrated. Lesions of the "intermediate" type did not differ from those found in the more typical lateral meniscus; the thin portion interposed between the femoral and tibial condyles was never injured. The "infantile" type often showed an incomplete transverse tear.

Mr. T. J. FAIRBANK, in a study of the knee-joint changes after meniscectomy, had compared the pre-operative and postoperative radiographs in 107 cases of meniscectomy, excluding all cases revealing pre-existing osteo-arthritis. Three groups of changes were found: a distally directed ridge at the margin of the femoral articular surface; flattening of the femoral condyle; and narrowing of the joint space. When this followed lateral meniscectomy, there was often some widening of the medial compartment. A study of elasticity curves of articular cartilage showed that a sustained load produced depression. Morning or evening radiographs of the weight-bearing knee showed its "space" to diminish by 1 mm. during the day. This joint compression must cause a transfer of load to the menisci in a centrifugal manner.

PERONEAL SPASTIC FLAT-FOOT

Dr. ROBERT I. HARRIS (Canada) and Dr. T. BEATH (U.S.A.) recalled that the deformity and stiffness in peroneal spastic flat-foot had long been ascribed to reflex muscle spasm from stimuli arising in the tarsal joints because of severe weak flat-foot. Electromyography revealed no spasm of the peronei; they were merely shortened, and deformity often persisted under anæsthesia. Sloman in 1921, and Badgley in 1927, had demonstrated calcaneonavicular coalition in some cases, and now a further anatomical anomaly had been found—namely, a talocalcaneal bridge comprising a process on the medial part of the talus meeting the posterior part of the sustentaculum. This anomaly, which could be revealed by posterosuperior radiography of the calcaneus, was found in 12 out of 17 cases of peroneal spasm; 3 of the remainder showed calcaneonavicular coalition, and the other 2 complicated rheumatoid arthritis. The bridge might be a synostosis or a coalescentia talo-calcanea, and, if the latter, either a syndesmosis or a synchondrosis. It had been observed by Pfitzner, who related it to the os sustentaculi. The authors considered that the cases with developmental bony anomalies showed no spasm, and that those with arthritis of the tarsal joints showed real spasm. In their opinion the following three types could be distinguished: rigid flat-foot due to talocalcaneal bridge; rigid flat-foot due to calcaneo-navicular bridge; and arthritic flat-foot with peroneal spasm.

Mr. S. A. S. MALKIN thought that a fourth group should be added: the adolescent spasmodic flat-foot following strain of the subtalar and midtarsal joints.

ASEPTIC NECROSIS OF BONE AFTER INJURY

Dr. EDWARD L. COMPERE (U.S.A.) spoke of the aseptic necrosis which may involve large intermediary fragments in fractures of the long bones. Regeneration resembled that of a bone-graft, and serial radiographs showed a temporarily increased density. Union normally occurred, but was delayed.

Dr. DALLAS B. PHEMISTER (U.S.A.), in dealing with the management of the aseptic necrotic head of the femur, recalled that in the adult such necrosis implied death of the overlying articular cartilage. At about 6–18 months, when it reached the part of the head opposite the upper acetabular margin, the fragile growing edge of tissue was apt to yield, so that the upper portion of the head broke off and collapsed under the stress of weight-bearing. With fracture of the femoral neck this happened only if the fracture united. To prevent this collapse, Dr. Phemister treated 4 cases of ununited fracture of the femoral neck showing aseptic necrosis of the head by threaded wires and the insertion of a tibial graft or grafts through the neck into the upper part of the head. In each case the fracture united, and extensive transformation of the femoral head took place without collapse, but the time was still too short for full assessment. With non-union of 3 years or more, a reconstruction operation or an arthrodesis was preferable. Tibial grafting had similarly been carried out, with seeming success, in a case of united femoral neck with early collapse of the necrotic head.

Mr. H. JACKSON BURROWS made a plea for prevention. Once cortical bone had been deprived of its blood-supply, delay in union was inevitable; worse still, once the cancellous end of a bone in an adult had died its articular cartilage was destroyed, and little or nothing could be done. Apart from proper handling of an injured limb, it was imperative to avoid unnecessary open operations, or, conversely, closed manipulations when open operation would be less damaging.

CERVICAL FRACTURE

Dr. WILLIAM A. ROGERS (U.S.A.) observed that treatment of cervical fracture or fracture-dislocation should aim at protection of the spinal cord and nerve-roots and fixation of the fracture. An emergency collar was used till skull traction could be applied. If the vertebral canal remained seemingly narrow, operation was performed—in the later cases under local anæsthesia. In 4 cases the vertebra above the lesion was lifted back by gripping its spinous process. Fixation with no. 22 stainless-steel wire was supplemented with bone chips, and the position was checked radiographically. Traction was continued for 3–5 weeks, and then walking was usually begun with a cervical brace. Of 32 patients, 21 underwent operation, bony fusion occurring in 20 in an average of 4 months. Those not operated upon received 10–12 weeks' traction followed by 6–8 months' cervical support. All patients walked finally without support, and 26 resumed full work.

Mr. E. A. NICOLL indicated that function depended not upon a good anatomical result but upon stability. Factors favouring instability were intervertebral-disc damage, rupture of the posterior spinal ligaments and

Digitized by Google

comminution of the vertebral body. Instability might demand operation. Simple compression-fracture of a vertebral body was stable, and its treatment was conservative. Fracture-subluxation with ruptured intervertebral disc and interspinous ligament was reduced in extension by gravity and could be treated conservatively, but it was important to avoid hyperextension. Fracture-dislocation with looked facets demanded open operation and grafting.

FRACTURE-DISLOCATION OF THE PELVIS

Mr. F. W. HOLDSWORTH had treated his 50 cases of fracture-dislocation of the pelvis, due to direct violence, after the manner of Astley Cooper, with a partially encircling towel held tight with weights and pulleys and with strapping traction on the lower limbs, or pin traction if one side were dislocated. Reduction was usually complete. The cases were followed over an average of 5 years. Of 27 with dislocation of a sacro-iliac joint 12 returned to heavy work, but 15 continued to have pain, which was referable to the joint; of 15 without sacro-iliac dislocation, 13 returned to work, and only 2 complained of persistent pain. This tended to improve with time, but its persistence for 2 years would demand consideration of sacro-iliac arthrodesis.

FRACTURES OF FEMUR

Dr. E. HARLAN WILSON (U.S.A.) had come to regard internal fixation with screws, and if necessary vitallium plates, as the treatment of choice for fractures of the shaft of the femur. After operation early movements were carried out, with sling suspension for 3–5 weeks. Sitting, or use of crutches by the younger patients, was allowed when the patient could extend the knee fully, flex it to a right-angle, and raise the limb against gravity. A normal range of movement was restored within six months.

LUMBAR DISC DEGENERATION

Prof. STEN FRIBERG (Sweden) had been able to confirm radiologically that the lumbar vertebral body above a ruptured intervertebral disc, especially the 4th, slid forwards on flexion and backwards on extension. In subjects examined soon after death degenerative changes were found to be most pronounced in the anterior parts of the discs, except the 4th and 5th where they were mainly in the posterior parts.

SCOLIOSIS COMPLICATED BY PARAPLEGIA

Dr. K. G. MCKENZIE and Dr. F. P. DEWAR (Canada) had found that scoliosis with paraplegia was usually congenital, sometimes idiopathic, and less often due to poliomyelitis, rickets, or neurofibromatosis. The deformity was severe; and myelograms might show a block at the apex of the deformity. Failing an early response to conservative treatment, operation should not be unduly delayed. The dura was found to be tightly stretched at the site of an angular deformity, compressing the spinal cord, which was not itself stretched. It was released by division of the dura.

PRESIDENTIAL ADDRESS

Dr. Harris recalled that the American Orthopædic Association was but eight years old at the time of Röntgen's great discovery. In 1912 Macewen had published his work on the growth of bone. Then had come the wars, and great advances with them. During all this time the general surgeon was gradually becoming the visceral specialist. There was a common meeting-ground for all branches of surgery in the basic sciences, research, and teaching. The claim of orthopædics to a special field of surgery carried responsibilities. Advance was possible over a much broader front than that of mere technical improvements. For instance, in histology there was the newer knowledge of intercellular substances; in biochemistry there was much to learn about osteogenesis, and endocrinology had something to contribute to this; the physiology of muscle-fibres needed further study; while in anatomy the relationship between structure and function could be investigated by modern methods.

RADIOACTIVE ISOTOPES FOR CLINICAL RESEARCH

MEDICAL RESEARCH COUNCIL STATEMENT

THE Medical Research Council have made arrangements to obtain from the United States Atomic Energy Commission limited quantities of certain radioactive isotopes for medical research, including therapeutic investigations. Further, it is expected that regular supplies will soon become available from Canadian and later from British sources.

The Council now invite institutions to submit for consideration detailed programmes of research in the clinical field. The application should include adequate information on the following matters:

(*a*) Specification of the radioactive isotope required.
(*b*) Quantity desired. (Radioactive isotopes with half-lives of less than 30 days may be allocated in fulfilment of one request, in amounts sufficient for six months' needs, with arrangements for shipments at intervals of not less than a week.)
(*c*) Date and rate of deliveries desired.
(*d*) Name of institution at which the materials will be used.
(*e*) Names and research experience of investigators who will use the materials. This list should include the names of the radiotherapist and physicist who will collaborate in the research.
(*f*) Purposes for which the materials will be used, with methods of administration and the dosage proposed.
(*g*) Protection and safety measures to be employed to safeguard the health of the workers. (Useful guidance will be found in the *Introductory Manual on the Control of Health Hazards from Radioactive Materials*, which may be obtained from the Council on application.)
(*h*) Proposed financial arrangements, including the sources from which the applicant will defray the cost of the materials.

Information under these headings, except (*h*), is required by the United States Atomic Energy Commission, as a condition for their supply of the isotopes. The Commission supply isotopes only for accepted lines of research the results of which are fully published, and which are conducted in institutions open to visits from investigators in this field of all nationalities. The Medical Research Council should be notified of any such visits by workers from other countries to any institution receiving the isotopes through their agency.

Progress reports must be made to the Council every six months. In the case of therapeutic investigations, the institution supplied with radioactive isotopes must undertake to register the patients treated, according to the cards and system of the Statistical Department of the General Register Office.

In its application to the Council for radioactive isotopes the institution is required to give the following undertakings:

1. That the materials supplied will not be used in any manner other than that disclosed in the application.
2. That the institution will maintain all necessary protection and safety measures to avoid the special hazards to health arising out of the possession, handling, and use of radioactive isotopes, and will allow inspection of all such protection and safety measures by representatives of the Medical Research Council.

The supplies of radioactive isotopes are at present limited and the materials are costly, especially on account of charges for transport.

It is expected that the isotopes in greatest demand will be radiophosphorus, P^{32}, and the radio-iodine, I^{131}. The following information about the preparations of these two isotopes available is given by the Commission:

Phosphorus 32

Half-life 14·3 days. Beta radiation 1·71 MeV. Supplied as phosphate ion, probably in the form of Na_2HPO_4, in a solution

Digitized by Google

containing 0·5–3·0 millicuries per millilitre. Chemical analysis is furnished with each shipment. Material will meet the following specifications:

Concentration	Greater than 0·5 mC./ml.
pH	7–9
Total solids	Less than 10 mg./ml.
Non-volatile matter	Less than 5 mg./ml.
P (inert)	Approximately 0·025 mg./mC. added. (Carrier-free material is available if desired.)
Cl	Less than 5 mg./ml.
Fe, Ni, Al	Content so low that no precipitate is formed at pH 7–9

Iodine 131

Half-life 8·0 days. Beta radiation 0·6 MeV. Gamma radiation 0·367, 0·080, and probably also 0·65 MeV. (10–15%). Carrier-free, in neutral or weakly basic solution containing 0·3–2·0 millicuries per millilitre. Chemical analysis is furnished with each shipment. Material will meet the following specifications:

Concentration	Greater than 0·3 mC./ml.
pH	7–9
Total solids	Less than 1 mg./ml.
Te inactive	0·1 mg./ml.
Te active	Less than 1×10^{-4} mC./ml.

The Council will not accept responsibility for the accuracy of the statement as to radioactive content which will accompany each sample, or for the freedom of the sample from toxicity.

The cost of the materials will depend on various factors, including the demand, but is unlikely in the first instance to be less than £1 per millicurie for I^{131} or 10*s.* per millicurie for P^{32}.

While every effort must be made to utilise these therapeutic developments and possibilities to the full, there can be little doubt that, from the long-term point of view, the treatment of cancer and allied diseases is most likely to be advanced by the encouragement of tracer investigations, using both radioactive and non-radioactive isotopes. Materials for this purpose are also obtainable from the Council, and at present, in view of the small quantities involved, no charge is being made.

The need for extreme caution in the clinical use of radioactive isotopic tracers cannot be over-emphasised. The safety of non-radioactive tracers should recommend their use in clinical investigations.

DANGERS AND LIMITATIONS OF RADIOACTIVE ISOTOPE THERAPY

Certain dangers inherent in radioactive isotope therapy are becoming recognised, especially in the case of radiophosphorus administered internally as inorganic phosphate. The most serious of these are possible injury to the reproductive organs, genetic damage, the induction of leukæmias and the hastening of the appearance of leukæmic conditions, and the production of malignant tumours. The leukæmogenesis and carcinogenesis, including induction of sarcoma of bone, are likely to be delayed effects, with a long latent period of possibly five years and probably often longer. Accordingly, in the present state of knowledge, it is usually unwise to employ radiophosphorus in the treatment of patients of either sex in the reproductive period of life or in patients where the expectation of life exceeds five years.

In general, it must be concluded that therapeutic trials of radioactive isotopes should be limited to cancer and allied diseases, and polycythæmia vera. With rare exceptions, radioactive isotope therapy should not be used in non-malignant conditions. Further, the opinion has been expressed that, in the present state of knowledge, radioactive isotopes should in no case be used in the treatment of children suffering from non-malignant diseases.

Despite these limitations, there is an important field for investigation in the therapeutic applications of radioactive isotopes. At first, it will be necessary to develop techniques and to confirm and extend the results of the American workers, while profiting from their experience. Subsequently, it seems likely that the development of selectively concentrated organic compounds containing radioactive isotopes may be a promising line of investigation. Probably there will be an immediate though rather limited field for the use of external applicators containing sources of beta rays. Experience with artificial gamma-ray sources, such as radiocobalt (cobalt 60), in radiotherapy is at present very restricted but this is a matter for experimental development when adequate regular supplies become available.

All correspondence should be addressed to the Secretary, Advisory Panel on the Allocation of Radioactive Isotopes for Clinical Research, Medical Research Council, 38, Old Queen Street, London, S.W.1.

Public Health

HYGIENE IN PALESTINE

ERIC HARDY
F.Z.S.

UNDER the British mandate, Palestine's sanitation and public health improved considerably from what they had been during the Turkish occupation. Scientific control of the mosquito-breeding places greatly reduced the amount of malaria-infested land, and the destruction of the packs of pariah dogs which had haunted the gates of the cities at sundown since Biblical times removed this dangerous source of rabies. In more recent years the Jewish settlements, with their technical advisers at the University of Jerusalem and elsewhere, developed parts of Lake Huleh, Jebel Usdum, and the plain of Jezreel which had previously been undeveloped malarious swamps. All this useful work is threatened by the disturbance of the civil war and the lack of scientific supervision of many of the native parts of the countryside.

The malaria position at the end of the mandate was roughly that the malaria risk was high in the Jordan Valley from the Syrian border to the south of the Dead Sea, chiefly on the Transjordan side. It was also very high in marshy parts of the coastal plain near the Wadi Sukreir, the Wadi Rubin, and the Tantura area, in the Wadi Faria near Nablus, and south of Faluja. Near Jericho, Tiberias, and Safad it was high from September to December but otherwise moderate; but there was little risk around Jerusalem, Hebron, and Lydda.

In 1940, Krikorian and Bedrechi listed 9 species in their *Atlas of the Anopheles Mosquitoes of Palestine*, published by the department of public health in Jerusalem, and a strict and wide control of mosquitoes in the villages was supervised in the later years of the mandate by Dr. J. MacQueen, the director of medical services, and Dr. W. K. Bigger, the A.D.M.S., with trained Jewish and Arab personnel, and also assistance from officers of the R.A.M.C. Together with Jewish scientists, a malaria research hut was maintained in the notorious Huleh region where the intensity of malaria in the Arab villages was very high, the splenic index being 80–100%, with an extremely high death-rate among children under 10 years, so that the natural increase of the population there was negligible. Lieut.-Colonel R. St. John Lyburn, R.A.M.C., describes[1] an experiment in the mass spraying of the Huleh villages, made with Dr. Bigger's supervision in January, 1946, primarily to control malaria and fly-borne dysentery, another widespread insect-borne trouble of Palestine which is likely to increase, since the native Arab practises little personal sanitation.

The three commonest rural malaria-carrying mosquitoes in Palestine are the palæarctic *Anopheles sergenti*, *A. superpictus*, and *A. saccharovi* (*elutus*), the last-named,

1. *Bulletin of the Jerusalem Naturalists' Club*, no. 14.

Digitized by Google

the largest anopheline in the country, breeding in swamps and stagnant water like Huleh. Many adult mosquitoes were found resting in the dark interiors of cattle byres and papyrus living-huts in the villages. The water is too cold for them to breed at Huleh (in the north) at that time of year, but the mosquitoes emerge to lay their eggs in the warmer weather of April. The malaria season lasts from then to December, when the mosquitoes become torpid again and are then more easily accessible for spraying.

Owing to the war-time development of the Palestine Potash Company's plant at the Dead Sea outbreaks of malaria were traced to the fresh-water swamps on the north-western shores of the Dead Sea at Ein Fashka, and these were controlled by cutting down the vast thickets of phragmites and arundo reeds and admitting light to the cleared channels of fast water from this well-known spring. Towards the end of the mandate D.D.T. had largely replaced the Paris Green hitherto used in breeding waters.

In October, 1942, a malaria survey of the Wadi el Arabah—the Arabah of the Bible, an arid desert over 100 miles long between the Dead Sea and the Red Sea—was made by Major Lumsden, during the active breeding season of the mosquitoes. He found both in the Ghor and the Wadi Arabah *A. superpictus*, the Ethiopian *A. d'thali*, *A. sergenti*, and *A. multicolor*. In February, 1946, an expedition of the Jerusalem Naturalists' Club to the Wadi el Arabah remained a fortnight there, when the mosquitoes were studied by Major F. Jacousiel, R.A.M.C. It was found [2] that even in this warm subtropical area mosquito breeding is at a very low ebb in February. A few scanty specimens of *A. sergenti* and *A. multicolor* were found, adult specimens of the first-named sheltering in a cave near the spring of Ein Arus in the Ghor. Larvæ of both species were collected in swamps in that neighbourhood, which is close to the south shore of the Dead Sea, and at Ein Weba, a small oasis in the heart of the Arabah desert. Of the culicine mosquitoes, the expedition found the large larvæ of *Theobaldia longiareolata* in sweet water at almost every spring and marsh visited in the Ghor and the Arabah, and a few larvæ of *Culex pipiens* were collected in the springs near Ein Beida. The latter species, with *C. laticinctus*, are the common urban culicine mosquitoes of Palestine, tolerating the very dirty water of ancient stone cisterns, Roman caves, concrete tanks and native wells, and they are abundant in native village houses. *Uranotœnia unguiculata*, *Taeniorhynchus buxtoni*, *Ochlerotatus caspius*, and *O. detritus* breed in the marshy parts of the country, and *O. mariæ* in saline water in holes by the sea. *Culex perexiguus* and *C. tritœniorhynchus* prefer cleaner water, but are common.

Other insect-pests, like small sand-flies (*Phlebotomus*) and house-flies (*Musca*), are probably as numerous as they naturally can be, and are less likely than the mosquitoes to be affected by the lack of scientific supervision.

Two Outbreaks of Typhoid Fever

On Clydeside

A sharp outbreak has occurred in the Greenock, Port Glasgow, and Gourock areas of Clydeside. By Sept. 5 the diagnosed cases totalled 29. The first 3 cases were in holiday-makers in Gourock who had crossed the Firth of Clyde to Kilcreggan, a favourite place for picnic parties, and there had drunk water (unboiled) from a stream. The next batch of cases came from members of a Church organisation, about 700 of whom went on an excursion to the same resort. Large numbers are known to have drank unboiled water from the stream and 24 cases have so far been notified. The remaining 2 cases are Greenock youths who were camping at Kilcreggan. All cases are due to *Salmonella typhi*. So far the organism has not been discovered in the stream; three samples taken have revealed 24 types of bowel organism but no typhoid organisms. It is known that drainage from a few dwellings reaches the stream above the point from which the water was taken, and samples of fæces have been sent for examination from 20 residents of these dwellings. The one food factor common to all cases is the consumption of water from this stream and it is almost certain that this is the source of the outbreak. A vigorous press campaign locally has been prosecuted to ensure that all possible cases are brought to light. It is anticipated that a few more cases will be detected, but the main outbreak seems to have passed.

In Shropshire

On Sept. 5 a night-sister at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry, complained of severe headache and was feverish; she had felt unwell the previous day. On Sept. 6 another night-sister and the assistant matron reported with the same symptoms. Next day there were 5 more cases, in a third night-sister, 2 day-sisters, and 2 maids. On the 8th and 9th positive Widal reactions were reported in 9 further members of the nursing and domestic staff, and in 2 children in separate wards who had been feverish since Sept. 5 and 6. Six nurses who went on leave on Sept. 3 and 4 have been reported as cases. Up to the night of Sept. 11 there were 24 cases among the nursing and domestic staff and 4 patients, and a further 3 cases have been confirmed among the outside domestic staff who had been sent home ill.

The signs and symptoms in all cases have been severe headache, temperature generally from 103 to 105°F at night and 100–101°F in the morning, injected conjunctivæ in most cases, and constipation. There have been no preliminary gastro-intestinal symptoms. The original diagnosis was influenza, but on Sept. 7, owing to the continued fever, Dr. Aylmer Lewis took a sample of blood for Widal reaction from a patient who had not had T.A.B. inoculations at any time and on the 9th this was reported as showing a titre of 1/125 for *S. paratyphi-A* and of 1/25 for *S. typhi*. Later samples showed a titre of 1/1000 for *S. typhi*; cultures of blood and fæces have so far been negative. The milk-supply has been investigated, samples of blood and urine and rectal swabs having been taken from all milk handlers at the farms supplying the hospital and from all the kitchen staff; samples of water are also being examined, and so far the distribution of cases and other factors suggest that the water-supply is the most likely source of infection. The population at risk in the hospital is about 400 patients, 170 nurses, 50 indoor domestic staff, 80 outdoor domestic staff, and 12 medical and clerical staff.

Paratyphoid at a Girls' Camp

A party of 42 members of the Oldbury (Worcestershire) branch of the Girls Life Brigade were camping in a small church hall in Pevensey Bay, Sussex, from Aug. 16 to 30, and since returning home many of them have developed paratyphoid fever. By Sept. 10 there were 19 suspected or confirmed cases in hospital. The church hall had main water and drainage, but with 6 adults and 36 girls in it the conditions must have been rather cramped and the lavatory accommodation and cooking facilities were in close proximity. Information was obtained from the local food office as to the main sources from which this party obtained their foodstuffs, and these were investigated, but nothing suspicious has been revealed.

One of the party, who had been doing the cooking, was taken ill with diarrhœa and vomiting about Aug. 22 and had to be suspended from cooking duties. She was removed to hospital for investigation, but by Sept. 11 it had not been proved that this was a case of paratyphoid fever. However, a small boy, aged 8, who had also been in the camp ill with diarrhœa, vomiting, and pyrexia on Aug. 22 was proved to have a paratyphoid B infection. It is understood that this boy had been isolated in the church hall, but under the existing conditions the isolation could not have been fully effective.

It seems probable, therefore, that this boy was the source of infection in the other cases. As to the origin of his infection it is unlikely that he contracted it in Pevensey Bay, since there have been no other cases there, and it seems probable that he was infected before his arrival on Aug. 16.

No secondary cases have arisen in Pevensey Bay up to Sept. 13.

2. *Ibid*, no. 20.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

THIS new impulse towards brightening our homes and persons is disquieting to sober conservatives like me. I suppose the urge started with women; after seeing the New Look (which gives them an old one) I can believe almost anything of the other sex. Not that men are altogether guiltless. There's that little matter of the patterned American ties, already mentioned in these columns.

I've always thought that men's clothes should be so quiet that nobody notices them. With these ties that's impossible: they yell at you. I own that I sometimes regret that I haven't a personality that could stand up to such a tie; I confess, too, that I have sourly envied the owners of these ties their American dollars or their American friends. But despite this emotional tinge I stand four-square by my principles—or did until the other night.

I was invited to a private party in honour of a much-loved American orthopædist. After our meal he made a little presentation to five British colleagues as a memento of their visit to him last year. The box was undone; and there, in vivid argument, were the five loudest ties in creation. The ties were donned. Do you know, they were actually very smart; and I felt dim and shabby. Anyone wanting a nice Paisley pattern in exchange for a quarrelsome multihued tie should get in touch with me. Only one thing worries me: surgeons, with their robust extroversion, can wear them all right; but can the physician with his more subtle and refined nature? We shall see. Meanwhile, I attract all eyes with the yellow waistcoat I bought next morning.

* * *

I was interested in what the Empire Conference on Scientific Information Services had to say about abstract journals; as was to be expected they emphasised the need for prompt publication and comprehensive coverage of the scientific journals. They even suggested that abstracts might be prepared from proofs of papers without awaiting their actual publication in the journals; if this arrangement could be applied to journals which publish preliminary reports, then abstracts would be as eagerly awaited as the 9 o'clock news. Better still, the research-worker could ring up abstracts every week or two and report verbally on his latest discovery. Promptness of publication of abstracts seems to be a soluble problem, but complete coverage is a more troublesome matter. It is not always easy to get a copy of the *Proceedings* (in Persian) *of the Society of Industrial Medical Officers of Abadan*, or of the *Compt. rend.* (in Polish) *of the Academy of Sciences of Pinsk*. But even when all the known medical and scientific journals are covered important gaps will still be left.

My wife is a careful reader of the *Daily Rapide*, and we often have the following sort of conversation. She looks up from the paper and asks, "Do you know that extract of dried bear's skin cures rheumatism?" I blush and admit ignorance. "Well, here it is: Prof. Stefan Ivanovitch of Irkutsk has cured hundreds of cases in this way and has increased Soviet productivity by 18%." Or it's Dr. Myron C. Jeggerts of Alabama who has cured peptic ulcers by making the patient stand on his head for 5 minutes daily. After these blows to my professional pride I look out for the further report in the usual journals and abstracts and of course find nothing there. I know the excuses the editors will offer: "How do I know the reports are true?" Surely we all know that our press is the finest and most reliable in the world; and when a newspaper has to print in four pages all the world's news, pictures, and advertisements it need not bother to publish lies. "Then why did not Professor Ivanovitch publish in the usual journals?" Why should he? He is a man of genius; he is not looking for academic promotion and does not need to have a minimum number and weight of reprints. He told the *Daily Rapide*'s correspondent and so reached the whole world and not merely a small coterie of unimportant biased and jealous "scientists."

Sir Isaac Newton discovered the differential calculus and never bothered to publish it at all; many orthodox scientists have sealed up the report of their experiments in an envelope which was not to be opened for 20 years, knowing the world was not yet ready to receive their message. Suppose a press correspondent had called on Newton, seen a MS. on his table full of hieroglyphics and inquired about it and been told "Oh, that is my differential calculus"; or if the correspondent was dining with the scientist and he happened to drop a hint about the contents of his sealed envelope. Surely it would be the bounden duty of the press in such circumstances to make known to the world the treasures that otherwise might have remained hidden. I am sorry that the Royal Society Conference did not arrange with the Newspaper Proprietors Association to keep abstracts informed of all scientific discoveries that receive their first publication in the lay press.

But even when the press is fully covered there still remains the "occasional" publication which must also not be neglected. A striking example has just come to my notice. From time to time I order a cask of cider from the Much Binding Cider Co. I read the accompanying literature with interest as it is pleasant to know the fine qualities of what you are going to drink. The other day I got an exciting special leaflet. One of the directors of the company had visited France and had come across a cider of most remarkable qualities; it was of liqueur type, of very high alcohol content, and would mature indefinitely; and then in large capital letters I was informed that it was a very potent *aphrodisiac* and so must be drunk in the strictest moderation. This was the discovery that the world—if not the scientific world—has been waiting for, and if I had not received the leaflet the world might never have known. Now I will have the laugh of all my pharmacological friends. While they go on frittering away their time on bits of isolated uterus or intestine or the hundredth anti-histamine or local anæsthetic I will be doing some critical experiments on this most beneficial and potent (that word should not be misunderstood) of therapeutic agents. It is true that I am not the actual discoverer; but it is not the discoverer but the man who makes the world believe in a discovery who receives the gratitude and plaudits of mankind.

* * *

One of the curious and inexplicable observations in our surgical life is the tendency of diagnoses to run consecutively. Perhaps for months we will not see a fracture of the femur, and then—presto!—one drops in of the shaft, a few hours later another of the neck, and perhaps the next day a compound one. Not an epidemic, I may presume, for they come from wholly unrelated parts of the country; but whether the moon was right, or whether the accident incidence was filled up and had to overflow at that particular moment I am never able to make up my mind.

Or perhaps we will not see a patient who needs a cæsarean for a considerable period. But then, if we have one, there are sure to be more close on its heels. And it is the same with other diagnoses. Lately the sigmoid has been the organ affected. We have seen diverticulitis, fatal and non-fatal, severe and mild, and carcinoma of the sigmoid in old and young (the last one at age 35) and in male and female. They have required simple excision, end-to-end anastomosis, abdomino-perineal resection, and all the variations of the surgical techniques mentioned in the books. When this is over, we may expect to see no more for months in our modest-size hospital.

* * *

We stopped for lunch at an American mess at Giessen. It had been the junior officers' quarters of a German army barracks. In the washroom my lay friend asked "What is that contraption, Doc?" On a pedestal was a round porcelain basin with a central drain about 6 inches wide. About a foot above on the wall were two handgrips. I had never seen anything like it before, but fortunately a memory from long-past classical studies gave me the answer. "That is a vomitorium," I said firmly (checking with one of the local boys, by the way, proved this was right). I had to explain its purposes. My friend looked at it with awe. "I always heard the Germans were thorough," he said, "but I had to see this to realise just how thorough they are."

Digitized by Google

Letters to the Editor

THE AGRICULTURAL WORKER

SIR,—By their article on Aug. 21 Dr. Keatinge and Mr. Littlewood have performed a service which has long been required. It is time that attention was focused on the social conditions of the workers who provide us with much of our daily food. I find it difficult, however, to believe that bigger farming units and a special medical service will provide the answer to the man-power problem. The authors say that the farm worker has little prospect of rising in the world. They mention the failure of the Government agricultural training scheme for ex-Servicemen, but not the fact that the Scottish Department of Agriculture has a waiting-list of over 10,000 for smallholdings, while Holland, Lincs, has over 800 ex-Service applicants.[1] The personal factor in ownership and responsibility therefrom is of considerable importance. Surely the provision of more smallholdings and small farms would attract greater numbers to the land, and offer the chance of rising in the world to those with the necessary ability. The authors' aggregation of farms into bigger units would presumably displace occupiers of smaller farms and might well displace other people from the land, as did the enclosures of the eighteenth century.

With the statement that small farms are uneconomic I am not qualified to disagree, but I would be chary of accepting the economist's yardstick for a way of life which is the vocation of the small farmer, and in connexion with a biological process which is so far removed from the mechanistic processes of industry. It appears to me that so many of the advantages of aggregation of units given by the authors, such as easier marketing and bulk buying, can be obtained equally well by coöperative methods, as among the smallholders in the Vale of Evesham.[2]

The writers state that the change from horse to tractor on the farm has made 200–300 acres of arable land the minimum for the efficient utilisation of implements and that "the present trend of scientific and mechanical invention, too, will increasingly favour larger units of production." Would it perhaps not be wise to adapt the machine to the man and develop the tractor or other farm implement according to the land and farm on which it will be used? The coöperative ownership by a group of farmers of the larger, more expensive, and less used items of machinery is a rather different matter from the aggregation of farm units, and is one which could easily be encouraged by the Government today. I find it difficult to see how such aggregation of farms would "facilitate the provision of scientific and technical advice." Is that not a question of availability of experts, or is it implied that "compulsion" would be more easily enforced with such aggregation? Education and example are methods more acceptable to the British temperament.

So many of the advantages claimed by the writers could be obtained by less revolutionary methods through the medium of education and existing village organisations. The Government are already tackling the housing problem, and much more could be done in this direction. Provision of water, sanitation, and power are other urgent requirements. Assurance of a just reward would probably do more than any other single measure to repopulate the countryside.

The authors propose a special medical service. Could not the existing country doctor carry out all the necessary examinations on entrants into agriculture and other supervision required, backed if necessary by a regional consultant service of specialists in agricultural medicine, or alternatively by a regional specialist with an interest in the agricultural aspects of medicine? Let us hope that it is not necessary to turn the whole structure of our countryside upside down in order to congregate our delicate farm workers into a large conglomeration of men and machines under the ever-watchful eye of an industrial doctor, perhaps also an industrial psychologist, and without doubt a foreman mechanic.

Let us remember that the "efficient," "economic," "large-scale," inorganic, monocultural system of agriculture, developed in the U.S.A. during the last and present centuries, has created one of the largest man-made deserts in the world. Perhaps the "dust bowl" of America cannot happen in this country, but let us not be complacent in our "can't-happen-here" attitude. Let us think much and experiment a lot before we throw overboard the traditional methods of agriculture which have maintained the soil of this island in an unequalled state of fertility and productivity over hundreds of years. Before we grub up our hedges, cut down our hedgerow timber, and grub out our yeoman farming stock let us be quite certain that we know what we are doing.

That is not to say that there is no place in English farming for large units. There have long been larger and smaller units, but the standardisation and industrialisation of agriculture is a conception fraught with danger. I should like to recall Sir George Stapledon's words in *The Land: Today and Tomorrow*: ". . . there is a grave risk of the family farmer being slowly and steadily swallowed up by large and fully equipped farming companies, and this to my mind would be the greatest ill that could befall the countryside."

Hitchin, Hertfordshire. ROBERT WIGGLESWORTH.

1. Massingham, H. J. The Small Farmer. London, 1947; p. 166.
2. *Ibid*, p. 134.

SALARIES IN GOVERNMENT SERVICE

SIR,—May I supplement the letter in your issue of Sept. 4? Since temporary M.O.s in the Ministry of Pensions do exactly the same work as the established officers, they are surely entitled to the same remuneration. No allowance is made to them, however, for the absence of pension rights, so they are underpaid vis-à-vis established officers to the extent of £150–200 per annum. Furthermore, should a temporary officer qualify for extra-duty allowance, he is given a bonus of 3% on his salary while his established colleague gets 8%.

Other injustices which should be ended are the recruitment and promotion of established officers while there still exist temporary officers with years of satisfactory service in the Ministry. Such officers should be taken on to the establishment and their pension rights back-dated. Moreover, this sensible method of recruitment would enable the Government to dispense with the services of some of the Civil Service Commission.

Now that the new Act is in operation, surely all Government medical services should be reorganised. At the moment many Ministry of Pensions officers are doing work which rightly is the Ministry of Health's, and on a salary scale below that of Ministry of Health officers.

TEMPORARY M.O. (PENSIONS).

STUDENT SELECTION

SIR,—As the number of methods of selection increases there is a growing tendency to forget certain fundamentals. Nobody overlooks the dilemma produced by an excess of candidates, but fewer and fewer people seem to realise that to deny an individual entry into a field of human endeavour which he is eager to join strikes at the very roots of human dignity. Since all short-time methods of selection are admittedly fallacious in a significant proportion of cases, I submit that equitable selection can be achieved only by raising the standards of training and by suffering a considerable degree of wastage.

If the supply of potential medical students far outstrips the demand is not this a splendid opportunity for obtaining an even better type of doctor by stepping up the intellectual and practical achievements demanded in the medical courses? Admittedly, at least in the beginning, this would involve a great wastage of those who fall by the wayside. But is it not foolish to think that a high level can be achieved without such wastage? A Minister who tried to ordain that all musical composition except that of masterpieces must stop would be regarded as insane. Yet this is exactly what we are doing in trying to cut out wastage of medical students. In a complex activity such as the practice of medicine nothing but an actual attempt can reveal the master and the inept.

Digitized by Google

Biology has shown us the only foolproof method of selection—that of trial and error and of survival of the fittest. This must remain the method of selecting future doctors if the standard of the profession is to go up and not down. Present difficulties may prevent us from giving full rein to this natural method, but at least we should not be blind to the viciousness of present-day restrictions. By making a virtue of necessity we are in danger of perpetuating an undesirable state of affairs. Any society which desires to have a sufficient number of people possessing the highest skills must be prepared to suffer wastage in training.

Usher Institute, University of Edinburgh. ERICH GEIRINGER.

EXSANGUINO-TRANSFUSION IN ACUTE LEUKÆMIA

SIR,—In his preliminary communication of Sept. 4 Dr. Piney says, "it is impossible to obtain very large quantities of blood at any one time in England." I do not understand on what grounds he makes this statement since he apparently did not apply to any of the regional transfusion centres. Had he done so, and if his patient belonged to one of the commoner blood-groups, his request could probably have been met without difficulty.

Experience so far acquired of exsanguination-transfusion in acute leukæmia suggests that this treatment has probably only a temporary effect. The decision to use it will, therefore, always be a difficult one, but should it ever become a recognised form of treatment it would be well to realise that the provision of the needed amounts of directly matched homologous-group blood will present great difficulty in certain cases. For example, group B and especially group AB, Rh-negative blood will be most difficult to provide in the quantities used in Dr. Piney's case, and group A and group O Rh-negative blood will not be much easier. Group O Rh-negative blood is always in great demand because part of the available supply (only about 7 out of every hundred donors belong to this group) is given to patients whose ABO and Rh groups have not for one reason or another been determined. Many of these patients are, in fact, Rh-positive, and some of them, though Rh-negative, belong to group A. If only the ABO group of these patients were determined, group A Rh-negative blood could be used instead of group O Rh-negative blood, thus lessening the constant drain on the latter. Considerable quantities of Rh-negative blood are, of course, used for the exsanguination-transfusion of infants with hæmolytic disease of the newborn.

It is improbable that any blood-bank could supply on demand sufficient Rh-negative blood for the type of transfusion described by Dr. Piney. In other words, such exsanguination-transfusions should always be deliberately planned in consultation with the regional blood-transfusion officer.

Ministry of Health, London, S.W.1. W. D'A. MAYCOCK.

SHORTAGE OF BLOOD FOR TRANSFUSION

SIR,—Since the war ended, the blood-banks have become progressively less well stocked with blood, presumably because, the fervour of patriotism having died down, donors are far fewer. I understand that the Ministry of Health makes itself responsible for rationing blood to hospitals and doctors, while the Medical Research Council looks after the needs of the research-worker. But practically no attempt is made to increase the number of donors, and so add to the stocks in the blood-banks. Of course, I must admit that some postal-cancellation stamps do inform us that blood donors are urgently needed, but it is doubtful whether many (or any) donors are obtained in this way.

My attention was forcibly called to the matter by Bessis and Bernard's [1] advocacy of exsanguino-transfusion in the treatment of acute leukæmia—a procedure which in the adult requires many pints of blood. The effects are so dramatic (although admittedly cure does not result [2]) that, having seen some of the cases in Paris during the meeting of the European Hæmatological Society, I wished to try it here; but there was not enough blood. One moribund patient was flown to Paris, and was given two exsanguino-transfusions, with the expected result—a remission.

Why, then, have the French so much blood, and we so little? The answer is to be found in the Gallic logic that is prepared to make use of the strength and weaknesses of men and women. Thus, every donor is given "chits" which entitle him to purchase extra rations. Now, as many members of the public imagine that it is weakening to give a pint of blood, they feel happier at being given the chance of making good the loss. And those who realise how totally harmless is the process are, nevertheless, delighted to get something more to eat. Then again, playing on the vainglory of everybody, each donor is given a card, signed by hand, thanking him for generously parting with his blood. And, on the back of the card, there is an appeal to the emotions: you have given of your blood as a gesture of our common humanity, and it may save the life of a woman in labour, of a child (perhaps your own), of an injured workman, and so forth.

There are many other useful hints to be gained by a study of the methods of the Centre National de Transfusion Sanguine, so admirably organised and run by Tzanck. For instance, the donors put their arm through a hole in a wooden partition, and so see neither the needle nor the blood; and everybody knows how much less it hurts if you do not see it. Propaganda, especially by posters, has worked wonders in France; why should it not do so here? The story is told of a man who tried to go to the head of a queue in Paris because, he said, "I have a blood donor's card." "Get to the tail," said everybody, "so have we."

London, W.1. A. PINEY.

1. Bessis, M., Bernard, J. *Bull. Soc. méd. Hôp., Paris*, 1947, p. 871.
2. Piney, A. *Lancet*, Sept. 4, p. 379.

CAUSE OF PRIMARY HEPATIC CARCINOMA

SIR,—The high incidence of primary hepatic carcinoma among Bantus [1] has not yet been explained. Kennaway [2] has shown that it is not due solely to racial factors, since the incidence in American negroes is not unduly high. Berman [3] has pointed out that in races having a high incidence of hepatic cirrhosis there is a high incidence of primary liver carcinoma and vice versa. In all communities primary hepatic carcinoma predominantly affects males,[4] and this is especially true of South Africa.[1] Where the incidence is high the disease occurs on an average at least 20 years younger than it does where the incidence is low. Berman also noted [5] that the hepatic cirrhosis on which the cancer supervenes is not multiple nodular hyperplasia due to acute necrosis but, as Stewart [6] had pointed out earlier, a more slowly progressive fibrosis, and that the cirrhosis antedates the cancer.

Of the suggested ætiological factors a number can be eliminated as not worthy of credence as direct causes—e.g., malaria, syphilis, alcohol, heredity, and trauma.[3] Many parasites have been blamed from time to time but few merit serious consideration. The trouble with most of them is that they are either too ubiquitous or not ubiquitous enough. Thus hepatic distomiasis could explain the high incidence in China but hardly in Uganda, and schistosomiasis is a scourge both where the incidence is high and where it is low. The same can be said of other parasites—coccidia, echinococcus, lamblia, *Cysticercus fasciolaris*—though the last-named has experimentally produced liver sarcoma.[7]

Chemical factors have aroused considerable interest since the discovery of the carcinogenic action of the aromatic azo compounds, *o*-aminoazotoluene and dimethylaminoazobenzene, and some other pure chemicals.[4] Yet there are difficulties about applying these experimental results directly to liver carcinoma in man. Thus these carcinogens will cause malignant tumours in other organs besides the liver—e.g., vesical papilloma

1. Berman, C. *S. Afr. J. med. Sci.* 1940, **5**, 54.
2. Kennaway, E. L. *Cancer Res.* 1944, **4**, 571.
3. Berman, C. *S. Afr. J. med. Sci.* 1941, **6**, 145.
4. Willis, R. A. Pathology of Tumours. London, 1948.
5. Berman, C. *S. Afr. J. med. Sci.* 1941, **6**, 11.
6. Stewart, M. J. *Lancet*, 1931, **ii**, 565.
7. Bullock, F. D., Curtis, M. R. *J. Cancer Res.* 1925, **9**, 425.

Digitized by Google

—though the liver is always directly damaged.[8] The proliferative changes after azo compounds are regenerative and there may or may not be a complicating or simultaneous cirrhosis. Indeed it is unlikely that an irreversible cirrhosis could be induced by dimethylaminoazobenzene, because of the rapid development of hepatomas. These observations do not concord with the observed cirrhosis-carcinoma relationships in man.

There is direct evidence that carcinogenic substances do occur in the human liver, but their nature and importance are uncertain. The investigations of Kleinenberg et al.,[9] des Ligneris,[10] Hieger,[11] and Steiner [12] can be summed up as follows:

Source of liver extracts	*Carcinogenic content*
Cancerous Bantu liver	Considerable amount
Non-cancerous Bantu liver ..	Moderate amount
Non-cancerous non-Bantu liver..	Little or none
Non-cancerous American negro liver	Little or none

The evidence suggests that these carcinogens are sterols and are not related to the aromatic azo compounds. Their origin is uncertain, but it is suspected that they are in some way connected with the diet. In my view there is a precise link between malnutrition and primary liver carcinoma in Africans, and a specific group of chemical carcinogens may be involved.

Attention has been drawn [13] to the frequency and importance of malnutrition in Uganda, where nearly every African child passes through a clinically recognisable phase of malnutrition, which may recur in adult life. In this condition there is fat infiltration in the liver,[14] which may progress to a cirrhotic condition, thus explaining in part the very high necropsy incidence of cirrhosis of the liver in East Africans.[15] Some other features of African pathology appear to be due indirectly to this malnutritional disease. In Uganda gynæcomastia is relatively common, and there is a high proportion of carcinoma of the male breast in East Africans.[16] With this gynæcomastia and tendency to carcinoma in the male goes a feminisation of the whole body; it is often difficult to sex the bones of Uganda Africans, and the testes are small and atrophic. There thus may be a connexion in Africans between liver derangements and feminisation of the male. In hæmochromatosis, feminisation, loss of hair, and impotence, with the testes often atrophic, are far commoner than is generally realised and in frequency come next to the classical triad of symptoms.[17]

The mechanism of this connexion appears to have been elucidated by Glass et al.[18] who showed that the cirrhotic liver could not inactivate œstrogens. Nor is cirrhosis necessary, for Hibbs [19] and Klatskin et al.[20] have described gynæcomastia in malnutrition. This can come about in two ways: the liver may be unable to inactivate œstrogens either because of vitamin-B deficiency [21] or because of a lack of lipotropic factors.[22] Malnutrition in East Africa is known to be associated with pathological changes characteristic of lipotropic-factor deficiency.[14 23] Thus from an early age the liver of malnourished Africans cannot metabolise œstrogens, which are retained in the body and produce feminisation. But œstrogens can induce malignant changes—sarcomata at the sites of injection, interstitial cell tumours of the testes, and carcinoma of the breast in both male and female mice [24]—and they can also cause hepatomas in male mice.[25]

It therefore seems reasonable to postulate that œstrogens might be the cause of the high incidence of hepatic carcinoma in Africans and in any other community where malnutrition and other causes lead to liver damage in young males. The effects would be less notable where liver damage occurs late in life. The accumulation of œstrogens in the African liver and their absence or comparative absence in the undamaged livers of American negroes and of white races would explain the known occurrence of carcinogens in some livers and not in others. On this hypothesis it is unnecessary to invoke other causes, such as parasites and such chemicals as the aromatic azo compounds which the primitive African would be unlikely to meet.

This hypothesis could easily be subjected to experimental proof, though I am not in a position to do this. The administration of œstrogens to male mice with dietetic liver damage or fibrosis should lead to a high incidence of liver carcinomata. If it is correct, the association between cirrhosis and carcinoma depends on the fact that it is only cirrhosis which will cause liver damage over a long enough period to allow carcinoma to develop.

This hypothesis arises out of work done at Mulago Hospital, Kampala, in conjunction with Dr. H. C. Trowell and Dr. E. G. Holmes. They are not responsible for the opinion expressed.

Bristol. J. N. P. DAVIES.

8. Orr, J. W. *J. Path. Bact.* 1940, **50**, 393.
9. Kleinenberg, H. E., Neufach, S. A., Shchabad, L. M. *Amer. J. Cancer*, 1940, **39**, 463.
10. des Ligneris, M. J. A. *Ibid*, p. 489.
11. Hieger, I. *Ibid*, p. 496.
12. Steiner, P. E. *Cancer Res.* 1942, **2**, 425; 1943, **3**, 385.
13. Trowell, H. C. *Arch. Dis. Childh.* 1937, **12**, 193. Trowell, H. C., Muwazi, E. M. K. *Ibid*, 1945, **20**, 110; *Trans. R. Soc. trop. Med. Hyg.* 1945, **39**, 229.
14. Davies, J. N. P. *Lancet*, 1948, **i**, 317.
15. Vint, F. W. *E. Afr. med. J.* 1931, **7**, 349.
16. Vint, F. W. *Lancet*, 1935, **ii**, 628.
17. Sheldon, J. H. Hæmochromatosis. London, 1935.
18. Glass, S. J., Edmondson, H. A., Soll, S. N. *Endocrinology*, 1940, **27**, 749.
19. Hibbs, R. E. *Amer. J. med. Sci.* 1947, **213**, 176.
20. Klatskin, G., Salter, W. T., Humm, F. D. *Ibid*, p. 19.
21. Biskind, M. S., Biskind, G. R. *Endocrinology*, 1942, **31**, 109.
22. György, P. *Proc. Soc. exp. Biol., N.Y.* 1945, **60**, 344.
23. Himsworth. Lectures on the Liver and its Diseases. Oxford, 1948.
24. Robson, J. M. Recent Advances in Sex and Reproductive Physiology. London, 1947.
25. Schenken, J. R., Burns, E. L. *Cancer Res.* 1943, **3**, 693.

M.R.C.P. EXAMINATION

SIR,—The membership is a test of ready general medical judgment. Since a consultant is one who is suddenly called to give a firm opinion on an unfamiliar case which has baffled those who are familiar with it, this is surely the right kind of test. There may be a place for another examination which demands a high standard in one department of medicine, but that is an inferior principle. "The era of the general physician is passing," according to your correspondents on Sept. 4. Have they never been at a loss to assign a case to its proper specialty? In the all-specialist era, who will be able to do this?

There is no logic or fairness in insisting on a three-year delay after qualification. In all examinations held on this imperfect earth, the undeserving will sometimes fluke his way through; how will it help us if he does so after some years of "experience"? The really good man, the one who is going to benefit most from his experience, will sometimes pass, fairly, just after qualification; why keep him down artificially?

The system of an important examination (like the title and the volume numbering of a periodical) ought to be preserved unless change is really imperative. Continuity is precious. If your two correspondents of Sept. 4 had their way, there would soon be two things, the Old Membership and the New Membership. Some would be sure the Old was better, and others that the New was better. Disputes and confusion would be inevitable.

If the results of the membership depend more on chance than they ought, the reason is not the system but the excessive number of candidates, which has certainly introduced a most undesirable atmosphere of pressure and haste. I suggest the following remedies:

1. The examination should still be held every three months, but no individual should be allowed to take it oftener than once in six months.

2. Really bad candidates should be referred for more than six months, the period varying with their ignorance.

3. If these measures did not suffice, the entrance fee could be increased and a substantial sum refunded for passing at the first or second attempt.

These measures would deter sportsmen from putting a bit on the membership as if it were a horse. To disavow personal bias, let me add that I mean to specialise, and that it was neither very soon after qualification nor at the first attempt that I became

ANOTHER M.R.C.P.

Digitized by Google

LETTER TO A NEPHEW

SIR,—The charming letter from an uncle to his nephew, published in your Students' Number is so very much out of date that I hasten to send you a more practical version:

My DEAR CHARLES,

You are more fortunate than I, for when I thought to enter the profession of medicine I had no near senior relative with whom to discuss this important decision. None the less, I am flattered that today any of the young should consult an ageing relative about the future.

Forty years ago, when I became a student, no one had the faintest prevision of the degeneration that was about to overtake not only the profession but the whole social life of the nation, during his working life. With the coming of Lloyd George's Panel Act certain wise men did predict a falling off in the status of the doctor and the standards of practice; but their forecast was an anæmic dream of what has actually happened. For with the passing of the Bevan Act, the whole of a great profession has been wrapped in complete subservience to the State, from which there is little likelihood of immediate escape. If they had become Civil Servants under the Act, there might have been some minor hope. But doctors have been made something far inferior to Civil Servants, and without their protective armour.

What you have to consider firstly therefore is this. The profession that you propose entering is undergoing a major upheaval. It is changing, via interference from the State, its whole system of practice, and the relations between doctor and patient are bound to alter accordingly. How exactly they will alter is not known; but the portents are bad. From your point of view you must, as a primary question, ask yourself whether you are prepared to take on your life work in what we will euphemistically call a "service." When the body of the profession were free men they gave service freely to their fellow men, following their own ideas of what was just and right. Yet there were always recognised services that could be entered by students after qualification, usually by further competitive examination. The Royal Navy, the Army, the Royal Air Force, the Colonial Service and its special branches like the West African; but above all, the finest service of its kind that has ever existed—the Indian Medical Service. But these services never had any gross excess of candidates in their most flourishing periods. Indeed, the Colonial Medical Service always had some difficulty in attracting sufficient candidates. In other words, the practice of medicine in a "service" has never appealed to any but a very small minority of those qualifying as doctors, for the very good reasons that the restrictions of a "service" have always been incompatible with the freedom of thought and action essential to the most intimate of all the professions.

Bearing this in mind, that you are not entering a free profession as in the past, but a departmental service of the State, you may contemplate in the abstract the ethics of the life of a doctor. You will find this very admirably set forth in the letter on p. 358 of THE LANCET of Aug. 28. But the picture there presented dates from before July 5, 1948, and even before 1913 when the first steps were taken down the old rotten weedy slope of State control. You must remember that your patients are going to look upon you now not only as some sort of a "doctor" but mainly as a mechanism through which they can obtain money as sickness benefit, medicine, and many other material things. And you yourself, if a practitioner, are going to find that if you attend to all the regulations and fill in all the forms you will achieve an easier existence by the miserable technique of least resistance. You will hardly have time to enter into your patients' difficulties and gain their trust as in the old days. This is the curse of a "service"!

But do not misunderstand me. There are and always will be those among us who *must* be doctors because any other life is intolerable to them. Some ot your background makes me think that you may be numbered amongst these happy few. They are not found in any special class or creed, though naturally more will be found to belong to medical families. At the present time there are large numbers of young men of wholly unsuitable type applying to be apprenticed to the profession, to gain a poor if reasonably certain livelihood, and under the delusion that it will give them some social status. If many of these are admitted, the status of the profession will become lower than it has ever been before, and its social position will be only in the annals of the past. The panel system of Lloyd George was fundamentally wrong, and has added less than nothing to the regard of the citizen for the profession. Now everyone has a "panel doctor" there is every reason to think that the position will be made immeasurably worse.

To help you to decide this vital question for yourself—and you alone can decide it—it will be useful to tell you what I should do if I had a son in the same dilemma. If the boy were a fool, I should let him do medicine if he wished, in the hope that he might acquire some sense and a living, though a poor one. But suppose he were a bright and intelligent type, I would go to any lengths to stop him throwing himself away on the desultory treadmill of the State. Yet if I were ultimately convinced, because he defied me and insisted on a medical career, that he was one of those who *must* be a doctor—just as there are those who *must* be a priest or who *must* be a veterinary surgeon—I should probably relent at the last.

So I can offer you no simple and easy way out of this thorny problem. But I can point out that there is one bright star ahead in a miserable world. You may even live long enough to see it, and if it comes to pass during your working life you may even be glad if you should choose the profession of medicine. The bright star that I see ahead is this:

The curiously mixed race known as the English have a passion for freedom, for doing their job in their "own damned tinker fashion." Whenever they have in their history become oppressed by a vile doctrinaire, be he Cæsar or Cromwell or James II, the English have thrown him off and his works, and reverted to their free way of life. Suddenly they see the great light of freedom, and in some manner they will rise up and throw off the present false claim of the State to direct their lives, and they will cast out their oppressors and their false gods, though they may starve and riot before they do it. Under such circumstances the practice of medicine will revert to its old system of a free life, and be carried on in the highly satisfactory manner that had obtained from Hippocrates to 1913. That light will be worth seeing.

Your affectionate uncle,

London, W.4. THOMAS NELSON.

IMPORTANCE OF FAT IN THE DIET

SIR,—The view has often been expressed that the vitality of the consumer is influenced by the level of his daily fat intake. Thus, the high fat intake of the American people is considered by Cruickshank [1] to be one of the factors responsible for their display of confidence. Conversely, the reduced fat intake of the British people is now alleged to be the cause, or one of the causes, of their present tiredness and proneness to fatigue. Bicknell [2] has written of the present diet being "hopelessly deficient in fat," adding that "lack of fat is why we are all worn out"; the same opinion has been expressed by Leyton.[3] Lord Woolton [4] has spoken of his certainty that the diet is dangerously deficient in fat, and Leitner [5] has discussed the diet's nutritional imbalance on that account. Others have written similarly. Since this belief has received considerable publicity, it might be profitable to examine how far it is supported by the evidence.

The average daily fat intake during the war years was reported to be about 80–100 g.[6]: at present it is stated to be about 60 g.[7] The first question is whether other war-affected communities consuming a reasonably adequate diet with a similar or lower fat intake displayed the same symptoms. In the Channel Islands,[8] during the occupation, the daily fat intake was about 40 g., and in Switzerland [9] during the war period it was 40–50 g.; yet reports indicate that a high level of fitness prevailed, particularly among the young. Next, it may be inquired whether communities whose normal fat intake is low are stigmatised by inferior vitality. The South African

1. Cruickshank, E. W. H. Food and Nutrition. Edinburgh, 1946.
2. Bicknell, F. *Med. Pr.* 1947, **217**, 381.
3. Leyton, R. N. A. *Brit. med. J.* 1948, i, 476.
4. Lord Woolton. House of Lords: Official Report, 1947, **147**, 400.
5. Leitner, Z. A. *Med. Pr.* 1948, **219**, 215.
6. Drummond, J. C. Nutritional Requirements of Man in the Light of War-time Experience. London, 1948.
7. Mills, G. T. *Brit. med. J.* 1947, ii, 926.
8. Banks, A. L., Magee, H. E. *Mon. Bull. Min. Hlth P.H.L.S.* 1945, **4**, 184.
9. Fleisch, A. *Schweiz. med. Wschr.* 1946, p. 889.

Digitized by Google

Bantu, whose fat metabolism is now being studied (this is the reason for our interest in this subject), when living on their customary diet, composed mainly of maize products and beans, consume about 30 g. of fat daily; they do not behave as "worn-out" persons. The Japanese,[10] hardly marked by tiredness or lack of self-confidence, are reported to consume 15–20 g. of fat daily. More remarkable, in the most prosperous regions of Java the daily fat intake is reported to be less than 10 g.; yet, according to van Veen [11] the inhabitants are in good nutritional condition.

Finally, in the only long-term fat-metabolism study on adult man, a subject consumed 2 g. of fat daily for six months,[12] and no pathological changes were observed in his blood, urine, or basal metabolism. Subjectively, the person felt less tired on the experimental diet than on his normal diet.

There is, of course, no desire to minimise the psychological, as distinct from the physiological, rôle of fat in the diet; the deprivation of fat to those habituated to a relatively high intake is undoubtedly a grievous hardship. But in view of the three types of evidence discussed, it is surely unjustifiable to define the deficiency symptoms of a nutrient whose minimum requirement is not yet established.

A. R. P. WALKER.

Nutrition Unit, Council for Scientific and Industrial Research, South African Institute for Medical Research, Johannesburg.

LIFE AND DEATH IN A CONCENTRATION CAMP

SIR,—I should like to comment on the report of Dr. Wolff-Eisner's book in your issue of Aug. 7. As a prisoner in the concentration camp at Auschwitz-Birkenau and later in a camp in Friedland near Breslau, I had opportunity to observe the consequences of famine.

I disagree with the statement that raw potatoes caused diarrhœa. On the contrary, in our camp we deliberately and successfully combated diarrhœa with raw potatoes. The effect was similar to that of an apple diet. Nocturia was not due to "irritable bladder" as Dr. Wolff-Eisner thinks; nor could it have been the consequence of incipient famine œdema, for nocturia and polyuria started from the first day in prisoners arriving from Slovakia in a good nutritional state. It was simply the consequence of food being given in the form of great quantities of soups—4–6 litres daily. Evidently such quantities of fluid could not be wholly excreted in the day-time, and the evening soup especially had to be excreted during the night as it would have to be by every healthy subject. In the later stages, of course, the elimination of œdema fluid in the horizontal position from the lower parts of the body contributed to the nocturia in a smaller degree.

Severe vitamin deficiencies were not observed, because potatoes, which are rich in vitamin C, and various other vegetables containing carotene and vitamins B and C constituted in most camps the bulk of the food (kohlrabi, white and yellow turnips, and red beet). It is not surprising, therefore, that in Dr. Wolff-Eisner's experience the addition of yeast had no remarkable effect.

Doctors coming to our camp from Theresienstadt believed, as did Dr. Wolff-Eisner, that deficiency of fat was an important cause of famine œdema, for addition of bacon to the diet caused the œdema to disappear. Perhaps a more plausible explanation is that this addition of fat calories saved body and blood protein from destruction and enabled the very small amount of protein in the food to be utilised. In all cases of famine œdema in our camp I found the chief cause to be lack of calories, although the protein intake (in the form of horse meat) during most of our imprisonment almost covered minimum requirements. But, as the calorie intake was always insufficient, body protein must have been destroyed to make up the required total of calories. The result was a fall in blood proteins, which in turn was the chief cause of famine œdema.

Presov, Czechoslovakia JURAJ ORAVEC.

10. Bourne, G. H. *Nature, Lond.* 1946, 157, 177.
11. van Veen, A. C. *Ann. Rev. Biochem.* 1942, 11, 391.
12. Brown, W. R., Hansen, A. E., Burr, G. O., McQuarrie, I. *J. Nutrit.* 1938, 16, 511.

HOMOLOGOUS SERUM HEPATITIS

SIR,—In the summary of his paper of June 19 (p. 941), Dr. Borensztejn claims that homologous serum hepatitis is transmissible to rabbits. This statement was based on an experiment in which the single rabbit inoculated intravenously with blood from a fatal case of jaundice died two months after inoculation and was found to have necrosis of the liver. The single control rabbit inoculated with distilled water remained well. In case it be thought that the problem of homologous serum jaundice has now been solved, I think it should be mentioned that blood from cases of infective hepatitis and homologous serum hepatitis have been inoculated into rabbits on numerous occasions by various workers in recent years with negative results. As an illustration, three experiments were carried out in 1942 at the Wellcome Institute in London. In the first, two rabbits were inoculated intravenously with blood from a patient with infective hepatitis; in the second, two rabbits were injected intravenously with blood from two cases of jaundice in soldiers of the U.S. Army who had received icterogenic yellow-fever vaccine; and the third pair received blood from two patients with jaundice following inoculation of an icterogenic pool of convalescent mumps serum. All these animals remained perfectly well over a period of a year.

F. O. MACCALLUM.

Virus Reference Laboratory, Central Public Health Laboratory, London, N.W.9.

SIR,—In view of Dr. Borensztejn's claim to have transmitted homologous serum hepatitis to a rabbit, some essentially negative work carried out in 1945 may be worth putting on record. Starting from the hypothesis that homologous serum jaundice was not caused by a virus, but was the result of sensitisation by some product of liver damage present in the injected serum, attempts were made to produce a similar disease in rabbits. Two rabbits were treated with carbon tetrachloride over a period of some days so as to produce progressive liver damage; when this was at its height serum was obtained from the animals and was inoculated into other rabbits. Blood samples were taken from these rabbits at weekly intervals and determinations of serum bilirubin were carried out. In all 16 rabbits were observed over a period of up to four months. The results were at first encouraging in that 10 animals showed a progressive rise of serum bilirubin up to a maximum of 1·67% in one instance, while one animal died of acute liver atrophy. As the work progressed, however, it became evident that the effects noted could not be attributed to the experimental processes but were most likely due to some extraneous factor such as a dietary insufficiency or the presence of some infective agent in the stock of rabbits, and the work was therefore discontinued.

While shedding no light on the ætiology of homologous serum hepatitis these results show that liver disturbance, progressing occasionally to acute necrosis, may occur in rabbits apparently spontaneously, and that claims to have transmitted the human disease to rabbits cannot be seriously entertained unless supported by observations on a much larger series of test and control animals.

D. J. BAUER.

Wellcome Laboratories of Tropical Medicine, London, N.W.1.

MAN INTO WOLF

SIR,—With regard to the annotation under this heading on July 10, I think it is of interest to quote Cervantes,[1] who, freely translated, wrote:

"To suppose that these northern people become she or he wolves is a very great mistake," said Mauricio, "although many believe they do."

"How is it, then," said Arnaldo, "that everybody says, and it is taken for certain, that in the fields of England are herds of wolves which are human beings so transformed?"

"Such a thing," answered Mauricio, "is impossible in England, for in that mild and very fertile country neither wolves nor any other kind of harmful animals such as serpents, vipers, toads, spiders, or scorpions can grow; it is well known that if any sort of harmful animal is brought to England, on arrival there it dies; and if from that

1. Los Trabajos de Persiles y Segismunda, book 1, chap. 18.

Digitized by Google

country any earth is taken to another country and a viper is encircled with it, the viper cannot escape from this imprisoning ring until it dies."

Spain's greatest writer of all time spoke here, as always, in friendly and sympathetic terms of England.

Santa Cruz de Tenerife. JOSE DURAN MOLINA.

POSTCRICOID PHARYNGO-ŒSOPHAGEAL PERFORATION DUE TO ENDOSCOPY

SIR,—In his article of June 26 (p. 985) Mr. Goligher discussed œsophageal and pharyngeal perforation during gastroscopy and œsophagoscopy. Most often perforation is the direct result of this operation, and takes place at the site of the pathological condition for which endoscopy has been undertaken. Occasionally, however, it is produced in the postcricoid region, at a point remote from the primary lesion. As only a few of these accidents have been reported, the following case may be of interest.

A man, aged 73, had for a year been vomiting and complained of difficulty in swallowing. X-ray examination of the œsophagus and stomach showed nothing abnormal. I attempted endoscopy 3 weeks before his admission to hospital, but I could not pass the œsophagoscope behind the cricoid cartilage. The day after his admission I tried again, and again had difficulty at the same place. After some time the instrument suddenly passed the cricoid cartilage, only to reveal loose connective-tissue instead of the œsophageal lumen. It was evident that I had perforated the posterosuperior part of the œsophagus, and shortly afterwards moderate subcutaneous emphysema appeared on both sides of the neck. Mouth feeding was stopped and nutrient enemas (250 g. daily) were given; subcutaneous saline (1 litre daily) and glucose saline (1 litre daily) were infused subcutaneously; and penicillin 25,000 units 3-hourly was started.

Except for slight tenderness on the right side of the neck there was no complaint, and 4 days later the subcutaneous emphysema had completely disappeared. The patient's temperature, however, immediately rose and remained between 100° and 102°F for the next week. The general condition was excellent; but despite complete absence of symptoms and signs a shadow at the base of the left lung was detected radiographically 6 days after the operation. Two days later the temperature rose to 102·8°F; tenderness at the right border of the larynx had increased a little, but there was no trace of infiltration or of air in the subcutaneous tissues, and laryngoscopy showed no abnormality. A mediastinal abscess was strongly suspected, and with local anæsthesia a collar mediastinotomy was done on the right side. The tissues were normal, but as my finger passed behind the cricoid cartilage into the mediastinum a large amount of pus and gas suddenly escaped. A rubber tube covered with gauze was introduced to the bottom of the cavity.

In 3 days the temperature fell to normal, but it soon rose again. Blood proteins and electrolytes, checked daily, were normal. During the ensuing days œdema appeared in the lower extremities and a hydrothorax developed on the left side; the chest was twice needled and 700 ml. of clear fluid evacuated. The patient died from heart-failure 24 days after the perforation.

Necropsy revealed a well-defined empty abscess cavity, 3·5–4 cm. in circumference, beginning behind and to the left of the œsophagus and reaching 15 cm. downwards, without any sign of communication with œsophagus, trachea, larynx, or plural cavities. In the œsophagus a carcinoma about 2 cm. in diameter was seen 3·5 cm. above the cardia. In the left pleural cavity 760 ml., and in the right 100 ml., of *clear* fluid was found; the lungs were œdematous. Between the layers of the pericardium adhesions, and in the coronary arteries arteriosclerosis, were noted; the valves were normal.

Goligher points out that "the anterior surface of the bony prominence provided by the cervical spine is seldom perfectly smooth, being marked by transverse ridges corresponding to the lower borders of the vertebral bodies, and in patients with spondylitis may be rendered extremely rough and irregular by the presence of pronounced osteophytes or spurs." In my case there was very pronounced spondylitis deformans with big exostoses along the borders of the cervical vertebræ; and these, together perhaps with not too skilful introduction, may have been responsible for the tear. I do not remember, $2^1/_2$ years after the accident, the position of the head; but, though generally I pass the instrument with the neck flexed, I probably tried all positions to overcome the difficulty encountered.

With our present knowledge it is obvious that in my case the amount of penicillin given (25,000 units 3-hourly) was insufficient; but even 100,000 units 3-hourly did not prevent the formation of a mediastinal abscess in the fatal case reported by Goligher. He suggests immediate suture of the tear, or, failing this, packing and drainage of the wound. Under similar conditions I shall certainly follow his advice.

KARSTEN KETTEL
Frederiksborg County Hospital, Hillerød, Denmark. Chief Surgeon, Ear, Nose, and Throat Department.

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SIR,—I was much interested in Mr. Cohen's remarks on the danger of injections being given into abnormal ulnar arteries. Both my own ulnar arteries are superficial, and, when having injections, I have had occasion to call attention to them. Perhaps an experience in a clearing station in July, 1916, may be of interest:

In a man with multiple injuries there were wounds of both forearms with hæmorrhage. The entry wound in the left arm was in such a position that I remarked that time would be saved if the ulnar artery happened to be superficial: it was and so was the one in the right arm. The next patient also had a wound of the superficial ulnar, the abnormality being one-sided. Then the anæsthetist looked at his own arms and found he also had one.

Six superficial ulnars in four people at one time—for in that rush the next patient was by the table ready for his turn.

Liverpool. GEORGE C. E. SIMPSON.

Obituary

SAMUEL WALTON WHEATON

M.D. LOND., F.R.C.P.

Dr. Samuel Wheaton, who died on Sept. 5 at the age of 86, was one of the few remaining medical inspectors of the old Local Government Board who had known Simon and other founders of English State medicine.

Wheaton qualified from St. Thomas's Hospital in 1886, taking his M.B. Lond. with honours the following year, and in 1888 his M.D. After holding an appointment as resident accoucheur at St. Thomas's Hospital he became physician to the Surrey Dispensary and to the Royal Hospital for Children and Women in the Waterloo Road. But in the midst of consulting practice his interest was aroused in the new specialty of public health—he had taken the D.P.H. in 1889—and in the early '90s he became a full-time medical inspector of the Local Government Board.

At first he was largely concerned with the control of epidemics and the improvement of sanitary administration, and to this period belong his notable reports on enteric fever at Atherton, diphtheria at Hinckley, and cholera at Ilkeston. Later under Sir Arthur Newsholme he was responsible for the administration of the board's new maternity and child-welfare service, and this work included investigations into the incidence and mortality of measles and pneumonia. Dr. Wheaton was also an assessor to the Miners' Welfare Committee.

Sir Arthur MacNalty, who was associated with Dr. Wheaton in his work at the board and later at the Ministry of Health, writes: "Samuel Wheaton was a wise physician, and he brought clinical experience to the service of public health. Though a little reserved in disposition, he was always courteous and considerate. With his bushy moustache and his broad-brimmed hat Wheaton looked rather like the conventional idea of an artist, and in fact a large portion of his leisure was spent in painting in oils. His pictures were often exhibited, and purple, blue, yellow, and green splashed boldly on his canvas showed his mastery of vivid and arresting colours. Even in the coldest of winters he refused to have a fire in his room; for he maintained

Digitized by Google

that this spartan way of life prevented the catching of colds."

In 1906 Dr. Wheaton was elected to the fellowship of the Royal College of Physicians, and from 1926 to 1928 he served on their council.

THE LATE PROFESSOR JAMIESON

MAY I add (M. J. S. writes) to the excellent pen picture of Jamieson drawn by two of his former colleagues in your columns something more about his life and work in Leeds, where for so many years he was an outstanding personality within and without the university? When I came to Leeds in 1910 Jamieson was still a demonstrator, but that modest title gave no inkling of his standing in the school, and that year, on Wardrop Griffith's translation to the chair of medicine, he became the first full-time professor of anatomy in Leeds.

During his 15 years' apprenticeship as demonstrator he had worked in close association not only with a physician-anatomist who was himself a brilliant teacher, but also with a succession of budding surgeons—Moynihan, J. F. Dobson, and William Gough—all of whom had been honorary demonstrators in the department. It is not surprising, therefore, that Jamieson's anatomical teaching was coloured by practical clinical considerations which added greatly to its value, particularly in a school which was mainly a training-ground for general practitioners and surgeons. As a teacher he was supreme. His lectures were attractive, lucid, and stimulating, but he was at his best in the dissecting-room, where, even after he became professor, he spent much of his time. Anatomy seems to attract or to breed good draughtsmen and good teachers, and his blackboard sketches were masterpieces of accuracy and clarity.

Jamieson had a long and varied experience as an administrator. His own department was exceedingly well managed and that without extravagance. In the earlier years of his professoriate he was also warden of Lyddon Hall, a hostel for men students. But it was during the 1914–18 war that he had his first real opportunity to show his capabilities. Professor de Burgh Birch, the dean of the medical faculty, was mobilised as a colonel of Territorials on the outbreak of war. Jamieson stepped into the breach, and for the next three years deputised for him. In March, 1915, he was himself commissioned as major and appointed registrar of the East Leeds War Hospital, a big organisation which began in part of the Township Infirmary in Beckett Street, and later extended to other institutions inside and outside the city. Later he was promoted lieut.-colonel and became administrator of the hospital. Meanwhile he continued to give part of his time to undergraduate teaching. These strenuous days brought him into closer contact with clinical colleagues and men in other walks of life than ever before. He took a particular interest in the welfare of the non-commissioned officers and men under his command—many of these war-time associates who turned to him for help in the post-war period are grateful for what he did for them. One of Jamieson's greatest pleasures was to take the chair at the annual reunion dinners of the hospital and to stand the first round of drinks. He rarely missed a meeting until he left Leeds in 1936.

In 1918, while still very fully occupied with his military duties, he was elected dean of the faculty of medicine and chairman of its board, complementary offices which he filled with distinction for 18 years of notable expansion. The school of dentistry (opened 1928), the extensions to the department of physiology (opened 1930), and the Algernon Firth Institute of Pathology (opened 1933) all owed much to his energy and drive. From 1923 to 1925 he was also pro-vice-chancellor of the university, and as this period coincided with a long interregnum in the vice-chancellorship Jamieson filled this office for the whole of the 1923–24 session.

He received degrees from both the institutions which he had served so well, the honorary LL.D. from Leeds in 1937, and later the M.A. and CH.M., jure officii, from Trinity College, Dublin. His portrait by Mr. Leo Whelan of Dublin, painted in 1937, is now in the medical school library at Leeds.

Jamieson had his own, sometimes unorthodox, methods or working. He was much given to writing memoranda on problems of the hour. These were never typed, except when duplication was essential, but were written in his own clear firm hand. Many of his colleagues have had reason to be grateful for these admirable documents, setting forth in lucid sentences the opinions of a man of vision and sound common sense. He never had a private secretary. The secretary of the school, or dean's clerk, as he was then called, had his own particular duties assigned to him—with a typewriter but no stenographer. Most of Jamieson's memoranda were written, not in the dean's office, which was much too public a place, but either in his own little sanctum with its private stair in the anatomy department or at home during the midnight hours.

In private life, despite certain appearances to the contrary, Jamieson was a sociable and friendly man. Like most people he had his antipathies, but fundamentally he was fair and tolerant, if given at times to the free and forcible expression of critical opinions. No teacher ever held a more assured place in the affection of his students, and his colleagues mourn the passing of a great teacher, a capable administrator and a loyal, warm-hearted, and courageous friend.

A memorial service for the late Mr. J. E. H. Roberts, consulting surgeon to St. Bartholomew's Hospital, will be held in the Church of St. Bartholomew-the-Less, West Smithfield, E.C.1, on Tuesday, Sept. 21, at 1 P.M.

Appointments

BENTHAM, FLORENCE, M.B. Durh., D.P.H.: M.O.H., Kettering.
ELEKTOROWICZ, ADAM, M.D. Lwow: radiologist, Bridge of Earn Hospital, Perthshire.

Middlesex Hospital, London:

KAVANAGH, STEPHEN, L.R.C.P.I., D.L.O.: acting otological registrar.
MONRO, R. S., M.B. Camb., F.R.C.S.: first assistant, professorial surgical unit.

Colonial Service:

FOSTER, W. S., M.R.C.S.: M.O. (health), Jamaica.
KAPADIA, K. K., M.B.: M.O., Seychelles.
SMITH, R. B. S., M.B. Durh., D.T.M., D.T.H.: asst. director of medical services, Northern Rhodesia.
STOBBS, J. E., M.B. Durh.: M.O., Nigeria.
URICH, L. G. W., M.R.C.S., D.T.M. & H., D.P.H.: deputy director of sanitary service, Trinidad.
ZAHRA, A., M.D., B.SC.: M.O., Nigeria.

Births, Marriages, and Deaths

BIRTHS

ADKINS.—On Sept. 6, the wife of Mr. E. W. O. Adkins, F.R.C.S.—a daughter.
HARDWICK.—On Sept. 3, in London, the wife of Dr. S. W. Hardwick—a daughter.
HENEGAN.—On Sept. 5, the wife of Dr. Donald Henegan—a son.
KELLY.—On Aug. 30, at Boscombe, the wife of Dr. Reginald Kelly—a son.
LEESON.—On Sept. 12, to Dr. Jean Leeson (née Mackay), wife of Dr. C. A. Leeson—a daughter.
MCCALL.—On Sept. 9, at Tunbridge Wells, the wife of Dr. Michael McCall—a daughter.
PEARSE.—On Sept. 4, in London, the wife of Dr. A. E. Pearse—a son.
PUNT.—On Sept. 14, in London, the wife of Dr. Norman A. Punt, F.R.C.S.E., D.L.O.—a son.
ROSS.—On Sept. 5, in Edinburgh, the wife of Mr. James A. Ross, M.B.E., F.R.C.S.E.—a daughter.
TAYLOR.—On Sept. 6, in London, the wife of Dr. G. R. Taylor—a daughter.
WHITE.—On Sept. 7, the wife of Dr. A. A. White—a son.
WILSON.—On Sept. 5, at Ludham, Norfolk, the wife of Dr. Peter Wilson—a daughter.

MARRIAGES

BROWN—HARDY.—On Aug. 27, at Great Sampford, Essex, Wilfred Stuart Brown, M.R.C.S., to Betty Stella Hardy.
LIVINGSTON—MCDONAGH.—On Sept. 9, in Jamaica, Sir Noel Brooks Livingston, to Josephine Olga McDonagh, M.R.C.S.
MATHEWSON—TIERNEY.—On Sept. 4, in London, John Gray Mathewson, M.B., to Jane Tierney.

DEATHS

BANKS.—On Sept. 9, at Hadlow Down, Sussex, Alfred Banks, F.R.C.S., D.P.H., aged 86.
KEMPSTER.—On Sept. 7, in London, Christopher Richard Kempster, M.R.C.S.
PULLING.—On Sept. 9, at Brighton, Herbert John Pulling, M.R.C.S., aged 88.
SONI.—On Sept. 7, in Manchester, Mul Raj Soni, B.A. Punjab, M.B. Edin., D.P.H.
WILLIS.—On Sept. 12, at Cheadle, Cheshire, Eugenic Leeson Willis, M.A., M.B. Camb., F.R.C.S.

Digitized by Google

Notes and News

PROF. JÖRGEN SCHAUMANN

ONE of the kindliest possible gestures has lately been made in honour of Professor Schaumann; a committee of fifteen clinicians has published a golden book [1] in his honour, and has persuaded Prof. Henri Gougerot, of Paris, to contribute a foreword setting Schaumann's work in its correct perspective. The work was to have been issued to celebrate Schaumann's 60th birthday, "mais les événements de l'époque ne permettaient pas de donner une suite immédiate á ce projet." The book contains over sixty reprints of articles which have appeared either in *Acta Dermato-Venereologica* or in *Acta Medica Scandinavica*; it is, of course, chiefly concerned with benign lymphogranuloma (Schaumann's disease) and with kindred topics. While Schaumann must feel pleasure in this well-merited distinction, others can be grateful for such a useful compilation of the writings of many eminent authorities now republished to honour one of the most progressive thinkers in modern European medicine.

REPRODUCTION EXPLAINED TO CHILDREN

Dr. Edward F. Griffith's *The Truth about the Stork* [2] is a good idea which does not quite come off. It was a useful inspiration that made him set out to describe human reproduction in clear, open, and easy terms to children; but he seems to be in some doubt about the age of the child he is enlightening. The book begins with anatomy and physiology explained in words suitable for a child of seven, but accompanied by pictures and diagrams which would be better understood by a ten-year-old. Again, these more or less scientific diagrams and photographs are interspersed with comic drawings of rabbits, germs, and Noah's ark only suitable for tiny children. Mating is simply described, and so is normal birth, but it seems unnecessary to go on, in a book of this kind, to breech birth, cæsarean section, abortion and miscarriage, venereal disease, sterility, and birth-control. These are subjects for the adolescent, not the young child—unless for some reason he asks questions, or has been frightened by something he does not understand, such as a miscarriage in his own family. Dr. Griffith, on thinking things over, may be inclined in future editions to turn his one book into two.

University of London

Prof. J. R. Learmonth has been appointed Heath Clark lecturer for 1949. He has chosen as his subject the Contribution of Surgery to Preventive Medicine.

University of Sheffield

On Wednesday, Oct. 13, Lord Horder will deliver the opening sessional address of the faculty of medicine, in the Firth Hall of the university at 3 P.M. His subject will be the Vocation of Medicine.

University of Glasgow

Prof. Geoffrey Jefferson, F.R.S., will deliver the Macewen lecture in the chemistry building of the university on Friday, Oct. 1, at 3 P.M. He has chosen as his subject the Contribution of Sir William Macewen to Neurosurgery and Its Sequels.

University of Aberdeen

Dr. H. W. Fullerton has been appointed to the regius chair of medicine in succession to Prof. R. S. Aitken who has been appointed vice-chancellor of the University of Otago.

Dr. Fullerton took his M.A. at Aberdeen in 1925 and his M.B. in 1931. In 1937 he obtained his M.D. with honours and four years later took the M.R.C.P. After holding a house-appointment at Aberdeen Royal Infirmary he was awarded successively Rockefeller and Beit fellowships. He is at present lecturer in medicine at Aberdeen and an assistant physician at the Royal Infirmary. He has published papers on the nutritional anæmias.

Royal College of Physicians of London

On Tuesday and Thursday, Oct. 12 and 14, at 5 P.M. at the college, Pall Mall East, S.W.1, Dr. Desmond Curran will deliver the Croonian lectures. He is to speak on Prefrontal Leucotomy.

1. Livre D'Or en l'Honneur du Professeur Jörgen Schaumann. Stockholm, 1948.
2. London: H. K. Lewis. 1948. Pp. 137. 6s.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty held on Sept. 6, with Prof. G. B. Fleming, the president, in the chair, the following were admitted to the fellowship:

John Bell Cochran, John Ernest Awelrydd David, Madhusudan Mohanlal Desai, Thomas Jack, Patrick MacArthur, Ronald Charles MacGillivray, William Greer Manderson, Ralph Adair Peebles-Brown, Nathan Sher (qua physicians); John Thomson Stanley Buchan, Reginald Wheeler Busschau, Thomas Lightbody Chapman, George Logan Clark, James Ross Hutchinson, Jacob Daniel Joubert, Anandlal B. Kothari, William Sommerville Mack, Pearl Anna Inglis MacLeod, Aaron Meyer Porter, William Rankin, Colin John Slight, William Barr Stirling, Alfred Edward Wilkinson, Robert Brash Wright (qua surgeons).

King's College Hospital

Prof. Henry Cohen will deliver the inaugural address of the session at the medical school on Friday, Oct. 1, at 3 P.M.

Westminster Hospital

The old students' annual dinner will be held this year at the Savoy Hotel on Saturday, Oct. 2, at 7.45 P.M. Sir Arnold Stott will be in the chair.

Middlesex County Medical Society

At a meeting of this society to be held at 4 P.M. today, Friday, Sept. 17, at the North Middlesex County Hospital, Silver Street, Edmonton, N.18, Mr. Ivor Lewis will give an address on Diagnosis.

International Scientific Film Congress

In connexion with this congress an exhibition of illustrations and photographs from teaching hospitals is to be held at 1, Wimpole Street, London, W.1, from Oct. 6 to 11. The exhibition is designed to interest medical teachers.

West London Medico-Chirurgical Society

A dinner of this society will be held on Friday, Oct. 22, at the South Kensington Hotel, 41, Queen's Gate Terrace, S.W.7, at 7.30 P.M. At 8.30 P.M. Dr. W. S. C. Copeman will give his presidential address on West London Worthies, a Retrospect.

British Hospitals Contributory Schemes Association

The final conference and annual general meeting of this association will be held at the Majestic Hotel, Folkestone, from Sept. 30 to Oct. 3. Mr. Aneurin Bevan will be the guest of honour at the dinner on Oct. 1, and the concluding business of the meeting will be to receive a report for the new association which it is proposed to establish.

Chadwick Lectures

The autumn programme of the Chadwick Trust includes lectures by Sir Arthur MacNalty on Advances in Preventive Medicine during the War of 1939–45 (Nottingham University College, Oct. 28, 4 P.M.), by Dr. Wyndham Lloyd on the Prevention of Tuberculosis with special reference to Environment (Westminster Hospital medical school, S.W.1, Nov. 2, 2.30 P.M.), and by Dr. Charles Seeley on Preventive Medicine and Clinical Medicine in relation to the Public Health (St. Mary's Hospital medical school, W.2, Dec. 2, 4.30 P.M.). Further particulars may be had from the secretary of the trust, 204, Abbey House, Westminster, S.W.1.

CORRIGENDA.—*Industrial-health Courses at Manchester:* The reference to these courses in the Students' Guide (Aug. 28) was incomplete. Courses for the D.I.H. are held each year at Manchester University, which was the first to offer a whole-time course for this diploma.

In the list of centres for the distribution of streptomycin (*Lancet*, Sept. 11, p. 428) the telephone number of Grove Park Hospital should be Lee Green 1077.

Diary of the Week

SEPT. 19 TO 25

Monday, 20th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Dr. Hedwig Kuhn (Hammond, Indiana): Eye Problems in Industry.

Wednesday, 22nd

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3 P.M. Dr. Paul Banzet (Paris): Surgical Treatment of Gastric Ulcers. (Bengue lecture.)

Friday, 24th

BIOCHEMICAL SOCIETY
11.30 A.M. (Department of Biochemistry, University of Sheffield.) Short papers.

Digitized by Google

SEPT. 25, 1948 PAGES 481 TO 516

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6526 LONDON: SATURDAY, SEPTEMBER 25, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Subacute Bacterial Endocarditis
Prof. CRIGHTON BRAMWELL, F.R.C.P. 481

Hæmophilus influenzæ Meningitis Treated with Streptomycin
P. M. SMYTHE, M.R.C.P. 485

An Artificial Heart or Cardio-pulmonary Machine
V. O. BJÖRK, M.D. 491

Absorption and Excretion Studies with Radioactive Penicillin
S. ROWLANDS, PH.D.
D. ROWLEY, PH.D.
H. C. STEWART, M.D. 493

Intestinal Obstruction due to Ascariasis
KHALID NAJI, B.M. 495

NEW INVENTIONS

Cannula for Repeated Intravenous Injections
T. G. OLOVSON, M.D. 495

REVIEWS OF BOOKS

Lecture Notes on Pharmacology. Prof. J. H. Burn, M.D., F.R.S. .. 496

Hutchison's Food and the Principles of Dietetics. Prof. V. H. Mottram, M.A., George Graham, F.R.C.P. 496

The Aseptic Treatment of Wounds. C. W. Walter, M.D. 496

DISABILITIES

13. Pulmonary Tuberculosis 507

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 509

PUBLIC HEALTH

Deadly Nightshade Poisoning ... 513

Typhoid Fever on Clydeside 514

LEADING ARTICLES

PENICILLIN IN SYPHILIS 497

HOW MANY NURSES ? 498

MYELOMATOSIS 499

ANNOTATIONS

Private Patients not Admitted .. 500

Radioactive Penicillin 501

Memorandum on Rh Factors ... 502

The Artificial Heart 502

Veterinary Progress 503

LETTERS TO THE EDITOR

M.R.C.P. Examination (Sir Henry Tidy, F.R.C.P.) 510

Handling of Food (Dr. W. S. Parker; Mr. R. F. Montgomerie, F.R.C.V.S.) 510

Supernumerary Nipples (Dr. H. M. S. Turner) 511

Intramedullary Nailing of Fractures (Mr. G. K. McKee, F.R.C.S.) 511

Binocular Microscopes (Dr. J. W. Shackle) 511

Spontaneous Rupture of the Rectum (Mr. A. S. Aldis, F.R.C.S.) .. 511

Blood for Transfusion (Dr. W. P. U. Jackson, Dr. K. S. Thompson; Dr. R. D. Popham) 512

International Congress on Population (Dr. Josephine Bruegel) 512

The Eosinophil Cell (Dr. R. E. Hope Simpson) 512

British Council Films (Mr. Paul Reed) 513

Dietary Fat (Dr. J.-Jacques Spira) 513

The Parkinsonian Smile (Sir Arthur Hall, F.R.C.P.) 513

Œstrogen and Blood-sugar (Dr. George Biro) 513

Medical Records 513

Primary Tuberculosis with Meningism 513

INTERNATIONAL CONGRESS OF INDUSTRIAL MEDICINE

The Law—Organisation of Industrial Medical Services—Medical Supervision in Industry—Incentives, Job Adjustment and Absenteeism—Work and Skill—Health and Disability—Hazards of Particular Industries—Occupational Tumours of the Bladder—Diseases of the Lungs—Toxicology—Atmospheric Pollution—Radiant Energy 504

PARLIAMENT

A Short Session 514

Defence Measures 514

The Farm and the Factory 514

OBITUARY

Eugénie Leeson Willis 515

NOTES AND NEWS

National Health Service 515

Selection of Nurses for a Mental Hospital 516

Royal College of Obstetricians and Gynæcologists 516

Royal Society of Medicine 516

Society of Apothecaries 516

Committee on Social Workers in Mental Health 516

Charing Cross Hospital 516

Welsh National School of Medicine 516

Institute for Scientific Treatment of Delinquency 516

Commonwealth Travelling Professorship 516

Diary of the Week 516

Births, Marriages, and Deaths ... 515

A SELECTION OF NEW LIVINGSTONE PUBLICATIONS

TEXTBOOK OF GENITO URINARY SURGERY
Edited by H. P. WINSBURY-WHITE, M.B., Ch.B., F.R.C.S. With 39 eminent contributors. 1062 pp. 451 Illustrations. 90s.

EMERGENCIES IN MEDICAL PRACTICE
Edited by C. ALLAN BIRCH, M.D., F.R.C.P. 278 pp. 113 Illustrations. 25s.

ORAL AND DENTAL DISEASES
Ætiology, Histopathology, Clinical Features and Treatment
By HUBERT H. STONES, M.D., M.D.S., F.D.S. R.C.S. 916 pp. 926 Illustrations. 90s.

TEXTBOOK OF THE RHEUMATIC DISEASES
Edited by W. S. C. COPEMAN, O.B.E., M.D., F.R.C.P. With 24 distinguished contributors. 620 pp. 351 Illustrations. 50s.

THE MODERN MANAGEMENT OF GASTRIC AND DUODENAL ULCER
Edited by F. CROXON DELLER, M.D., M.R.C.P. 208 pp. Illustrated. 20s.

MANUAL OF LEPROSY
By ERNEST MUIR, C.M.G., C.I.E., M.D., F.R.C.S.E. 216 pp. 70 Illustrations. 17s. 6d.

Please write for a copy of our Catalogue giving details of all our books and journals. If you will indicate your interest we will keep you informed of special books.

E. & S. LIVINGSTONE, LTD. *Medical Publishers*, Teviot Place, EDINBURGH

Digitized by Google

Dietary Deficiencies

Although there seems to be no evidence of severe malnutrition in this country at the present time, there are, in individual cases, manifestations such as lack of concentration, lassitude, chronic fatigue and nervous disorders, which appear to be caused by inadequate diets. Some of these symptoms may be signs of a deficiency of the B vitamins.

Marmite is a yeast extract containing naturally-occurring riboflavin (1.5 mg. per oz.) and niacin (16.5 mg. per oz.) as well as other factors of the B_2 group derived from yeast; these include pyridoxin, pantothenic acid, choline, biotin and folic acid.

The dietetic value of Marmite has long been recognised; it is prescribed extensively as a prophylactic measure in combating malnutrition.

MARMITE

YEAST EXTRACT

Jars: 1-oz. 8d., 2-oz. 1/1, 4-oz. 2/-, 8-oz. 3/3, 16-oz. 5/9
Obtainable from Chemists and Grocers

Special terms for packs for hospitals, welfare centres and schools

Literature on application.

THE MARMITE FOOD EXTRACT CO. LTD.
484/2 35, Seething Lane, London, E.C.3

Brand's Essence (of Meat)

. . . has been recommended by doctors for over 100 years. It contains 10% of soluble meat protein, is free from fat and carbohydrate, and has a low salt content.

Because it is rapidly absorbed, owing to the perfect state of solution of the protein, it makes no demands on the digestive system and can be given in cases of acute digestive disorder. Brand's Essence is unrivalled as an aid to convalescence after serious illness. From chemists, 3/- a jar.

PROTECTING YOUNG TEETH

In recommending a dentifrice for children's use, three major factors will influence your selection.

(a) It is of obvious importance that the cleansing agents employed should be completely free of abrasive action.

(b) Powerful astringents are contra-indicated, as these may irritate and inflame the gum membrane.

(c) The essential oils incorporated must have a pleasant appeal to the young patient.

In all these respects, Phillips' Dental Magnesia presents a dentifrice which can, with confidence, be recommended to children of all ages. Completely free from harmful ingredients, it possesses a unique flavour which makes a very strong appeal to the young. Phillips' Dental Magnesia has, moreover, the outstanding property of inhibiting oral acidity by reason of the 'Milk of Magnesia'★ content, a very real advantage in protecting young teeth.

Phillips' Dental Magnesia (Regd.)

THE CHAS. H. PHILLIPS CHEMICAL CO., LTD. 1, WARPLE WAY, LONDON, W.3.

★ *'Milk of Magnesia' is the trade mark of Phillips' preparation of magnesia.*

Digitized by Google

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

SUBACUTE BACTERIAL ENDOCARDITIS *

CRIGHTON BRAMWELL
M.A. Camb., M.D. Manc., F.R.C.P.
PROFESSOR OF CARDIOLOGY IN THE MANCHESTER UNIVERSITY

THE successful treatment of subacute bacterial endocarditis with penicillin is one of the most remarkable advances in therapeutics in recent years. Five years ago this was an incurable disease; no known drug, not even the sulphonamides, could influence its course, though it appeared that spontaneous recovery took place occasionally. Now we may expect to control the infection in most cases, provided diagnosis is not unduly delayed.

Subacute bacterial endocarditis is a common cause of death in patients with chronic rheumatic heart disease and congenital heart disease. Laws and Levine (1933) found that it was responsible for death in 29% in their series of cases of rheumatic heart disease, and Abbott (1932) stated that it was the cause of death in 33% of patients with congenital heart disease.

In 1944 the Medical Research Council initiated, at twelve centres in Britain, an investigation of the treatment of this disease with penicillin, and Christie (1948) has reported the results obtained in 269 cases so treated. My department in Manchester participated in this investigation, and the present paper is based on the first 50 cases we treated. These may be divided into two groups:

First Series.—33 cases treated before June, 1946, and reported by my colleagues Jones et al. (1947). This may be regarded as a fair average sample of the disease. All 33 cases have now been followed up for not less than two years.

Second Series.—17 cases treated since July, 1946. These are in a rather different category, for many of them had previously failed to respond to treatment elsewhere, and must therefore be regarded as less favourable from the therapeutic aspect.

DIAGNOSIS

It is convenient to subdivide bacterial endocarditis into acute and subacute. Some cases may be regarded as chronic, but these do not appear to differ ætiologically from those classed as subacute, and clinically there is no sharp dividing line between the two.

Acute endocarditis does not concern us here—it is rather to be regarded as a complication of some other disease. In pneumonia, for example, Luxton and Smith (1943) have shown that bacterial endocarditis is much less rare than is generally supposed. It may be an important cause of death, but it generally escapes recognition during life, its manifestations being overshadowed by those of the more obvious pulmonary lesion. The acute cases, in which the infecting organism is commonly a hæmolytic streptococcus, a staphylococcus, a pneumococcus, or a gonococcus, run a rapid course and generally prove fatal within two months.

In subacute bacterial endocarditis, on the other hand, the site of primary infection is in the heart itself, the disease runs a more chronic course, and, in the great majority of cases, the organism concerned is *Strep. viridans*.

The principal clinical features on which we are accustomed to base a diagnosis of subacute bacterial endocarditis are a valvular lesion or congenital defect, pyrexia, embolic phenomena, splenomegaly, and a positive blood-culture.

The Pre-existing Lesion.—The orthodox view, in the past, has been that subacute bacterial endocarditis rarely attacks a heart which has not previously been damaged by rheumatic infection or is the seat of some congenital abnormality, but it is remarkable that the pre-existing heart disease is almost always trivial, and that patients with advanced heart disease appear to be immune. For example, auricular fibrillation was present in only one of the 33 patients in our first series and in only 5 of Christie's (1948) 269 cases. Likewise none of our patients gave a history of heart-failure before infection, and in only 3 had there been any considerable impairment of capacity for effort; even these 3 carried on their normal activities. Of the remainder, 17 were in employment, and 11 women looked after their homes and families. The other 2 patients were still at school or college. In 13 of our patients there was a complaint of dyspnœa on unusual exertion but not during ordinary activity, while in 17 there had been no impairment of exercise tolerance and 8 of these did not even know that they had heart disease.

Of our 33 patients, 29 had rheumatic heart disease, but in 11 of them systolic murmurs only were present on admission. So rarely does one hear a typical crescendo presystolic murmur in bacterial endocarditis that its presence is sufficient to make one question the correctness of the diagnosis. Of our 12 rheumatic cases that came to necropsy in 2 only had the mitral disease produced stenosis. Aortic incompetence, on the other hand, was common, being diagnosed clinically in 16 of the 29 rheumatic cases. Coombs (1922–23) and Starling (1922–23), in their papers on chronic bacterial endocarditis amongst ex-Servicemen from the 1914–18 war, both remark on the rarity of a history of rheumatism and on the fact that often there was no evidence of previous cardiac damage.

Pyrexia.—Unexplained pyrexia in a patient with chronic heart disease is a pointer, and may be the only pointer, to the diagnosis of subacute bacterial endocarditis. It calls for immediate blood-culture. On the other hand, the absence of pyrexia does not exclude the possibility of infection, for in the more chronic type of case there may be long apyrexial periods. In one patient who was under my care in hospital some years ago, and in whom the diagnosis of subacute bacterial endocarditis was confirmed at necropsy, the temperature never rose above normal during the last nine weeks of life. The possible absence of pyrexia has been emphasised by both Coombs (1922–23) and Starling (1922–23).

Embolic Phenomena.—Major embolic phenomena may involve either the arteries of the limbs or those of the internal organs. In our series cerebral, splenic, renal, and coronary arteries were involved. Minute emboli lodging in the skin or subcutaneous tissues produce petechial hæmorrhages and Osler's nodes, whereas those lodging in the glomeruli of the kidney are one of the causes of hæmaturia in this disease.

Splenomegaly may be due either to infarction or to toxæmia. In the past most clinicians have taught that in congestive heart-failure the spleen is rarely palpable, and that in chronic valvular disease clinical enlargement of the spleen indicates infection. Fowler (1947), however, has brought forward evidence based on necropsy findings that the spleen may be considerably enlarged in heart-failure associated with rheumatic valvular disease. Taking 200 g. as the upper limit of normal and 300 g. as the lower limit of palpability, in 15% of his cases of congestive failure the spleen should theoretically have been palpable, though in only one case had it actually been felt during life.

Blood-culture.—Libman (1913), Osler (1908–09), Horder (1908–09), and the earlier workers generally were of opinion that in this condition blood-culture often proved negative. With the improved modern technique it is our experience that a positive blood-culture is obtained on the first attempt in the great majority of cases. In the 50 cases in our combined series the organism was isolated in the first blood-culture in 43, in the second in 5, in the fourth in one, and in the remaining case a positive culture had previously been obtained in another hospital. The technique is important and has been described by Penfold et al. (1940). In 5 cases in which, before the

* Based on a paper read at the Derby Medical Society on March 16, 1948, with further follow-up of cases to June, 1948.

Digitized by Google

patients came under our care, repeated blood-cultures had been negative we were able to isolate the organism.

To observe the response to penicillin it was important that only proved cases of subacute bacterial endocarditis should be treated. Hence, for this investigation, cases in which we failed to obtain a positive blood-culture were excluded from the series. While these observations were in progress, 4 such cases, which clinically were regarded as subacute bacterial endocarditis, were admitted to my wards. In 2 of these, in view of the gravity of the patient's condition, treatment with penicillin was started after only one blood-culture had been taken. Of these 4 patients 2 died, and in them the diagnosis of bacterial endocarditis was confirmed at necropsy; the other 2 recovered.

To sum up, therefore, in 52 proved cases of bacterial endocarditis, a positive blood-culture was obtained on the first attempt in 44, on the second in 5, and on the fourth in one, while in 2 cases blood-culture proved negative. There remain 2 cases in which the diagnosis seemed highly probable on clinical grounds but in which blood-culture was negative. If we accept these 2 as bacterial endocarditis, blood-culture was positive in 50 and negative in 4, in 2 of which only a single culture was taken.

Patent Ductus.—I cannot leave this aspect of the subject without referring to a group of cases of special interest, in which the underlying lesion is a patent ductus. In such cases, of which there were 2 in our series, both children, the embolic phenomena involve the pulmonary instead of the systemic circuit, producing recurrent pulmonary emboli. The importance of this group, as Gilchrist (1948) has shown, is that the infection can often be controlled by ligature of the ductus without penicillin, though in patients who are gravely ill a course of penicillin may diminish the surgical risk.

TREATMENT

Early in this investigation it became evident that the duration of treatment was of great importance. Of 52 patients (Christie 1948), all given 5 mega-units of penicillin, 83% relapsed or died infected when the treatment lasted only five days, compared with 50% of those who were given the same total quantity of penicillin in ten days, and 22% of those in whom the period of treatment was twenty days. Later it was found that a dose of 0·5 mega-unit daily for twenty-eight days was sufficient to control the infection in 90% of patients. This was the dose given in all but 3 of the patients in our first series who lived to complete treatment.

We have usually given penicillin by three-hourly intramuscular injection, and this has been well tolerated for long periods. In 5 cases we used a continuous intramuscular drip, changing the site every twenty-four hours; but in each case, after a few days, we were obliged to resort to injection owing to severe pain at the site of the drip and the development of pyrexia. In all these cases the penicillin was of the less purified type, and we have not tried this method with the more highly purified preparations now obtainable.

The progress during treatment in a typical successful case may be summarised as follows:

The temperature falls to normal within a few days, but the pulse-rate takes much longer to settle. The patient should be confined to bed for three weeks after the end of treatment, though the temperature and pulse-rate are normal. Carefully graduated and cautiously applied bed exercises are then started, and about ten days later the patient is allowed up for a short time. Great care is necessary during the early period of rehabilitation following successful treatment, however well the patient may appear to be when resting in bed. In fact we regard gradual rehabilitation in this disease as no less important than in myocardial infarction, undue haste being likely to lead to heart-failure.

Though infection can usually be controlled by a single course of treatment lasting only twenty-eight days, it takes much longer for the erythrocyte-sedimentation rate (E.S.R.), the anæmia, and the weight to return to normal. In our successful cases the E.S.R. did not reach normal until about five weeks after the end of treatment. There was often little rise in the hæmoglobin percentage during treatment, but subsequently steady improvement took place and a normal level was attained, without transfusion, about three months after the end of treatment; a gain in weight continued up to nine months after treatment. In 8 of our successful cases the gain in weight averaged 23 lb.

Convalescence in these patients is slow and requires careful management. In our cases the average period in hospital was fourteen weeks; full activity was rarely resumed sooner than six months after the end of treatment.

In cases in which the infecting organism is highly resistant to penicillin, Christie (1948) has suggested that 2 mega-units daily should be given for six or eight instead of only four weeks, but we have not yet made sufficient observations to assess the efficacy of this dosage.

In one of the patients in our second series in whom the organism was known to be highly resistant much larger doses were given; but, though these temporarily controlled the infection, a relapse occurred on each occasion when the penicillin was discontinued.

This patient had been treated elsewhere with the usual routine course of 0·5 mega-unit for twenty-eight days but had not responded. In his second course of treatment, which lasted eighty days, we started with 1 mega-unit daily and subsequently increased this to 3 and later to 8 mega-units. It was only on 8 mega-units that blood-cultures became negative. After relapse, a third course was given, consisting of 12 mega-units daily for twenty-nine days. This controlled the infection, but four days after the completion of this course the patient again relapsed, and died two months later. This man received a total of 720 mega-units in six months.

In several of our cases, though the temperature fell to normal after treatment had begun, it rose again at the beginning of the second week, and an intermittent pyrexia persisted until the penicillin therapy was discontinued, when, in every case, the temperature became normal. At first we were inclined to suspect that this pyrexia indicated failure to control the infection, and we therefore doubled the dose of penicillin, but, instead of falling, the temperature then rose higher. These observations led us to conclude that, when the temperature falls to normal in the first week, a subsequent rise in the second week is a drug fever.

The only other toxic manifestations of penicillin in our series were urticarial rashes in 2 cases and thrombocytopenia in 2 others.

RESULTS

Of the 33 patients in our first series 15 died and 18 are alive. Of those alive 15 are free from infection two years or more after the end of treatment; one is at work but has not been re-examined; one has recently received a course of treatment in a London hospital after reinfection with a different organism; and one has been readmitted with a reinfection following a dental extraction performed without penicillin cover.

We feel hopeful therefore that most of these cases will prove to be permanently cured, for Christie's (1948) figures show that 90% of relapses occur within a month of the end of treatment. In our first series, in cases treated with a full course of 0·5 mega-unit for twenty-eight days there were 2 reinfections (see above) but no relapses. In our second series, 3 patients did not respond to penicillin, and there have been 2 relapses. Of the patients who relapsed one died infected; and in the other blood-cultures were negative for fifteen weeks before death from heart-failure.

The degree of recovery can be gauged from the fact that, of our 18 patients who survived, 13 have resumed

Digitized by Google

their previous occupations without any evidence that their capacity for exertion has deteriorated; one is not working, since there is no economic necessity for her to do so; one is receiving treatment for a reinfection; and 3 have subjectively deteriorated and are unfit for work. These last 3 are the only patients in whom cardiac enlargement was progressive after the end of treatment. In one of them, in whom only an aortic lesion had been present, signs of mitral stenosis developed, and in the other 2 the cardiogram showed an increased tendency to right axis deviation. These changes suggest that in some cases, even after the infection has been controlled—in fact in the process of healing—a stenotic valvular lesion may develop or increase in severity; thereby throwing an additional and progressively increasing burden on the heart.

PROGNOSIS

Duration of Infection.—The most important factor in prognosis appears to be the duration of infection before treatment. In our first series, when symptoms had been present for less than ten weeks before treatment was begun no patient died, whereas none with symptoms lasting for thirty weeks or more recovered. A similar tendency is apparent in the combined series (Christie 1948), though the contrast is less striking. From these figures the importance of early diagnosis is obvious. The sooner treatment is started, the greater is the prospect of success.

Unfortunately at this stage of the disease diagnosis may be extremely difficult, for the initial symptoms of bacterial endocarditis give little indication of the nature of the infection; in our cases the commonest presenting features were lassitude, generalised "rheumatic" pains, pyrexia developing in patients already under observation, or a vague illness resembling influenza. In 3 cases major embolic accidents marked the onset of symptoms: in one of them a subarachnoid hæmorrhage was presumably due to rupture of a mycotic cerebral aneurysm; in a second hæmoptysis from a pulmonary infarct led to a mistaken diagnosis of pulmonary tuberculosis; and in the third visible hæmaturia and loin pain from a large renal infarct suggested a urinary calculus. Persistent sweating or pallor were the presenting symptoms in 3 cases. In the more chronic type of bacterial endocarditis described by Starling (1922–33) anæmia was a much more prominent symptom, the average hæmoglobin value in his cases being only 55%, but in these cases infection had probably been present for a longer time when the patients first came under observation.

Generalised "rheumatic" pains were a common symptom in our patients. They were of sudden onset but fleeting, and were rarely confined to the joints but often affected muscle masses in the limbs or trunk. Such pains are apt to lead to a mistaken diagnosis of "rheumatism" or even of rheumatic fever.

Age.—Christie (1948) states that "age was of doubtful prognostic significance, except in the group over 50." In our combined series there were 9 patients over 50, 3 of whom are still living. The higher mortality among the older patients may be partly due to the fact that in them the condition is more apt to escape recognition, hence the infection remains untreated for a longer time.

Heart-failure.—As I have already remarked, the pre-existing heart lesion, whether rheumatic or congenital, is usually trivial, and it is not until infection has been present for a considerable time that heart-failure appears. When it is present it adds greatly to the gravity of the prognosis (see below).

Nutrition.—Christie (1948) emphasises the importance of the state of nutrition as a factor in prognosis, and the need for a high-calorie diet, as in other protracted fevers. The significance of nutrition appears to be independent of the duration of infection or of the incidence of heart-failure.

CAUSE OF DEATH

Of the 33 patients in our first series 15 died, 8 during or within a few days of the end of treatment, the other 7 between four and thirteen weeks after treatment. In the whole series of 269 cases (Christie 1948) there were 131 deaths.

In those who died during treatment infection was considered to be wholly responsible for death in one case and partly responsible in 4. In no case in which death took place after treatment was there any evidence that infection played a part in the fatal issue.

Heart-failure was directly responsible for death in 5 of our 15 fatal cases and was a contributory cause in 5 others. Heart-failure usually developed when considerable cardiac enlargement was present, and there was a definite relation between (1) heart size and death-rate, and (2) heart size and duration of infection before treatment. Patients with large hearts generally gave a history of symptoms of infection lasting over many weeks whereas those without cardiac enlargement had been ill a shorter time. This direct relation between the duration of the bacterial endocarditis and the heart size suggests that cardiac damage due to the infection plays an important part in producing cardiac enlargement and heart-failure

Admittedly, various degrees of cardiac enlargement were present before infection, but the high degree of cardiac efficiency in most of our patients before infection suggests that their cardiac lesions were comparatively trivial, and that most of the cardiac damage was due to the subsequent infection.

Recovery was the exception in those who developed failure and the rule in those who did not. At the onset the failure was usually left-sided. Both myocardial and valvular damage due to the infection were factors in producing failure, but the mechanical stress from valvular lesions probably played the more important part.

Major vascular accidents, cerebral hæmorrhage in 2 cases and pulmonary embolism in one, were the cause of death in 3 of our cases. In one of these the fatal hæmorrhage appeared to be attributable to cerebral embolism which had occurred twelve months earlier.

Renal complications were considered to be partly responsible for death in 4 of our patients, 3 of whom died before the end of treatment.

PREDISPOSITION

In our first series there were 11 men and 22 women, and it is remarkable that in 7 of the women infection developed during pregnancy. The first 2 of these, in whom infection had been present for a considerable period before treatment was begun, both died; the other 5 were treated early and did well in spite of major vascular accidents in 2 and heart-failure in one. In one case a macerated fœtus was expelled a few days before the beginning of treatment, the other six children are well. Thus, provided the infection is promptly detected and adequately treated, the prognosis is good for both mother and child; and since, owing to the association of heart disease with pregnancy, these patients are usually under supervision at the time infection occurs, there is every opportunity for early diagnosis.

This very high incidence of subacute bacterial endocarditis during pregnancy calls for explanation. It is true that, in my clinic, we are particularly interested in heart disease associated with pregnancy, and that the material passing through our maternity hospital is carefully screened from this point of view; but, even making allowance for this, we feel that some other predisposing factor must be involved, and that in this disease, as Coombs (1922–23) suggested, the soil may be even more important than the seed.

The high incidence in pregnant women recalls the high incidence of "endocarditis lenta" among Army

Digitized by Google

pensioners after the 1914–18 war. When I was medical registrar at the Manchester Royal Infirmary in 1920–23, this disease was so common among ex-Servicemen that I nicknamed it "pensioners' heart." I can recall on two occasions seeing three necropsies on a single morning.

In 1923 Coombs (1922–23) reported 30 cases of "endocarditis lenta" seen since the end of the first world war. He distinguishes "endocarditis lenta" from the more acute type of bacterial endocarditis by the fact that it runs a course of months or years (one of his patients lived for over three years), that there is little or no fever, and that necropsy reveals anatomical evidence of stubborn opposition to the infection.

Of his patients 29 were males. A few acute cases in women, running a course not exceeding three months, were seen at the same time, but there was only one woman in the more chronic group. Of the 29 males 22 had served in the army, and 80% of these had been infantrymen or gunners with an average period of service of more than three years, mostly in France. Coombs says they were "men of fine physique and morale, men who joined the army early, served with all their might, and exerted themselves to the utmost limit of their physical powers." By contrast he did not encounter a single case among men of indifferent physique, whose service had been at the base and elsewhere, at home or overseas. He concludes that "so constant is the relation between physical fitness and strenuous exertion on the one hand, and proneness to endocardial infection on the other that a belief in the causal relation between the two can hardly be avoided." He suggests that excessive fatigue from the strenuous exertion to which these men had been subjected may have predisposed the body to infection. Possibly some similar predisposing factor may explain the high incidence of the disease during pregnancy. If this be so, it may provide a clue to the line of investigation we should pursue in searching for prophylactic measures.

The increased incidence and the more chronic nature of the disease among ex-Servicemen is emphasised by Wauchope (1925), who reviewed 125 cases of subacute and chronic bacterial endocarditis which came to necropsy at the London Hospital in 1907–24, and 70 cases, in 37 of which a positive blood-culture was obtained, admitted to hospital in 1911–23 in which no necropsy was performed. The number of male patients seen in 1922 was greatly in excess of that in previous years, whereas there was no corresponding increase in female cases. The increased incidence was due entirely to ex-Service cases. The sudden increase in 1921–22 is explained by the fact that before 1921 many Service patients were still in the army and treated in military hospitals. The reversion to the pre-war incidence in 1923 was sudden. Neither Coombs (1922–23), Starling (1922–23), nor Wauchope (1925) offers any explanation of the fact that the disease in ex-Servicemen generally runs a more chronic course than in civilians.

The same was true in Germany. Curschmann (1922) reported that at the Rostock Clinic the average number of fatal cases of subacute bacterial endocarditis in the three five-year periods between 1900 and 1915 was 8. In 1916–20 it rose to 15, and in 1921 there were 12 cases, an increase of more than 700% over the peace-time incidence. It is significant that after the 1939–45 war there was no corresponding exacerbation of "endocarditis lenta." This was a war of movement as contrasted with the static conditions of trench warfare in 1914–18. Chronic infections such as "trench foot" were less prevalent, and verminous infestation had been largely eliminated.

"Endocarditis lenta," as seen in ex-Servicemen of the 1914–18 war, presents some interesting points of contrast to the type of subacute bacterial endocarditis we see today. Its course was more chronic, the febrile disturbance was less pronounced, and often there was no rheumatic history nor evidence of any pre-existing valvular or congenital lesion. These features suggest that the infection had attacked a previously healthy heart and was not superimposed on a pre-existing lesion. This makes one wonder whether, in view of the trivial nature of the pre-existing heart disease in some, at least, of the subacute cases, the supposedly "rheumatic" lesion may not in reality have been produced by *Strep. viridans* rather than by previous rheumatic infection. This hypothesis is supported by the fact that rheumatic infection of the mitral valve generally leads to stenosis but mitral stenosis is rare in subacute bacterial endocarditis, being present in only 2 of our 12 supposedly "rheumatic" cases which came to necropsy.

SUMMARY

A favourable response to penicillin may now be expected in about half the patients with subacute bacterial endocarditis; but by earlier diagnosis we should be able to improve on that figure.

Early diagnosis is often difficult, and I suggest that, in every patient with unexplained pyrexia, especially if there be an associated heart lesion, a blood-culture should be taken without delay.

The longer the infection is allowed to run on, the greater the damage to the heart, and consequently the greater the risk of heart-failure, which is the principal cause of death.

There is a second reason why early diagnosis is so important. The pre-existing heart lesion is generally trivial and, if only we can bring these patients under treatment before the infection has had time to produce further damage, we may reasonably hope to render many of them fit to resume their former occupations.

Unfortunately, in some cases, a progressive valvular stenosis develops, in the course of healing; in fact the cure of the infection appears to be directly responsible for the aggravation of the valvular lesion. At present we have no means of dealing with this complication, but perhaps our surgical colleagues may be able to help.

The high incidence of bacterial endocarditis during pregnancy may prove to be a clue to the line of investigation we should pursue in searching for preventive measures to combat this disease.

The discovery of penicillin has opened a new chapter in the story of bacterial endocarditis. There are other chapters waiting to be written.

I am indebted to Dr. Morgan Jones, Dr. R. W. Fairbrother, and my other colleagues who have participated in this investigation.

REFERENCES

Abbott, M. E. (1932) Nelson Loose Leaf Medicine, vol. VI.
Christie, R. V. (1948) *Brit. med. J.* 1, 1.
Coombs, C. F. (1922–23) *Quart. J. Med.* 16, 309.
Curschmann, H. (1922) *Münch. med. Wschr.* 69, 419.
Fowler, L. O. (1947) *Ann. intern. Med.* 27, 733.
Gilchrist, A. R. (1948) *Brit. Heart J.* 7, 1.
Horder, T. (1908–09) *Quart. J. Med.* 2, 289.
Jones, A. M., Herring, R., Langley, F. A., Oleesky, S. (1947) *Brit. Heart J.* 9, 38.
Laws, C. L., Levine, S. A. (1933) *Amer. J. med. Sci.* 186, 833.
Libman, E. (1913) 17th Internat. Cong. of Med. Sec. VI, Med. 196.
Luxton, R. W., Smith, G. S. (1943) *Quart. J. Med.* 12, 61.
Osler, W. (1908–09) *Ibid*, 2, 219.
Penfold, J. B., Goldman, J., Fairbrother, R. W. (1940) *Lancet*, 1, 65.
Starling, H. J. (1922–23) *Quart. J. Med.* 16, 263.
Wauchope, G. M. (1925) *Ibid*, 19, 35.

"... In the supreme question which faces our generation, physics and chemistry and engineering have no answers for us. They are ethically neutral. They are preoccupied with physical matter. They can give us more horsepower; only the naïve, however, will claim that horsepower can develop within itself the means by which our runaway technologies can be brought under control. They can help more men to better health and longer life; but they have little relationship to the problem of discovering a new set of human purposes, or to the art of human relations, or to the winning of social and moral wisdom, upon which peace and successful government depend."—R. B. FOSDICK, Rockefeller Foundation Review for 1947, p. 9.

Digitized by Google

HÆMOPHILUS INFLUENZÆ MENINGITIS TREATED WITH STREPTOMYCIN

P. M. SMYTHE
M.B. Camb., M.R.C.P.
FIRST ASSISTANT AND REGISTRAR TO THE CHILDREN'S DEPARTMENT, THE LONDON HOSPITAL

UNTIL recently *Hæmophilus influenzæ* meningitis was usually fatal. Duncan and Webb (1934) found only 27 recoveries reported, 70% of them being in patients over the age of 2 years. A slight improvement followed the introduction of sulphonamides and Fothergill's horse serum, but results remained unsatisfactory. The first big advance was Alexander's combined therapy with sulphadiazine and specific anti-influenza-B rabbit serum. Using this method she reported 68 recoveries out of 87 cases (Alexander 1944), Smith et al. (1946) 24 recoveries out of 27, Beck and Janney (1947) 19 out of 22, and Turner (1945) 10 out of 20.

The introduction of streptomycin was a further advance. The National Research Council (1946) reported 87 recoveries out of 100 cases, but some of these had received combined therapy; Weinstein (1946) 7 out of 9; and Alexander et al. (1946) 18 out of 21, 3 of whom were not controlled by streptomycin and were given rabbit serum and sulphonamides as well.

Penicillin in conjunction with sulphonamides has also been used, particularly in this country. The largest series so treated is that of Zinnemann (1946) who reported 8 recoveries out of 15 cases. I record here the results in 12 cases transferred to the London Hospital for treatment with streptomycin. In 10 of them penicillin or sulphonamides had been administered before admission; but these drugs had not controlled the infection and *H. influenzæ* was still present in the cerebrospinal fluid (C.S.F.) or blood.

Dosage and Treatment.—A routine of treatment was followed in conformity with the recommendations of the Medical Research Council committee for streptomycin trials in non-tuberculous conditions. All the patients received about 20 mg. of streptomycin per lb. body-weight daily, divided into six intramuscular injections, together with a daily intrathecal injection of 25–100 mg. in 5 ml. of saline, the dose varying with the age of the patient and the severity of the disease. Treatment by both routes was continued until the C.S.F had been sterile for at least a week. No other specific treatment was given unless there was no response to streptomycin. Blood-transfusions were given when indicated for anæmia. Feeding was by œsophageal tube if there was any disturbance of consciousness.

Streptomycin Levels.—The methods of titration of streptomycin in blood-serum and C.S.F. were in accordance with Medical Research Council's instructions (M.R.C. 47/241, May 8, 1947). In 2 cases the serum-streptomycin level was estimated. An hour after the intramuscular injection of 80 mg. the concentration was 8–16 units per ml., and four hours after injection 2–4 units. The C.S.F.-streptomycin levels estimated twenty-four hours after intrathecal injection are shown in table I. After the injection of 25–50 mg. the level was usually 8–16 units per ml., and after 100 mg. it was 32–64 units per ml.

Toxicity.—Streptomycin caused no toxic effects, and there were no reactions from intrathecal instillation. One child (case 8) appears to be moderately deaf after a nine-day course of streptomycin, but whether this resulted from the drug or the meningitis, or both, it is impossible to say.

Bacterial Sensitivity.—In estimating sensitivity of *H. influenzæ* to streptomycin two methods were used. At first the minimal inhibiting concentration of the drug in Fildes's broth was estimated. This was 1 unit per ml. in 2 cases, and 2 units in 1 case. It was soon recognised that the results obtained by this method varied considerably with the size of the inoculum and the constitution of the medium. Latterly two drops of a solution containing 100 units of streptomycin per ml. was placed in a cup in the agar plate, and the diameter of the surrounding zone of inhibition was measured. This was done in the remaining 8 cases from which an organism was grown, and the zone of inhibition in these was 15–23 mm. in diameter.

Sensitivity tests were repeated whenever organisms reappeared in the C.S.F. In 3 cases that relapsed the

TABLE I—RESULTS OF TREATMENT OF *H. influenzæ* MENINGITIS WITH STREPTOMYCIN

Case No.	Sex	Age (yr.)	Days ill before start of streptomycin	Intramuscular streptomycin (mg. daily × no. of days)	Intrathecal streptomycin (mg. daily × no. of days)	Ave. range of C.S.F.-streptomycin level (u./ml.)	C.S.F.-sugar (mg./ml.)	C.S.F.-culture (no. of days† positive)	Sensitivity of organism	Blood-culture	Clinical severity	Result
1	M	9/12	19	500 × 10	25 × 8	4–8	..	+ (1)	<2 μ per ml.	..	Mod.	Died
2	M	9/12	31	600 × 7	100 × 7	32–64	35	–	–	–	Mod.	Mental defect
3	F	9/12	21	500 × 28‡	50 × 2 25 × 12	16–32	30	+ (3)	21 mm.	Con.	Mod.	Good
4	F	1	10	400 × 8	50 × 8	2–4	..	+ (1)	Sens.	+	Mod.	Good
5	F	1	8	500 × 14	50 × 11	8	30	+ (1)	15 mm.	+	Mod.	Good
6	F	1	15 Rel.	400 × 8 400 × 11	50 × 8 100 × 5 50 × 6	8 32–64	.. ..	+ (1) + (1)	23 mm. 15 mm.	+ +	Mod.	Good
7	F	1	12 Rel. Rel.	500 × 10 500 × 7 500 × 12	50 × 10 50 × 7 50 × 11	8–16 8 8–16	20 53 32	+ (1) + (1) + (3)	Sens. Sens. 20 mm.	+ – +	Sev.	Good
8	M	1 4/12	5	500 × 9	50 × 9	2–8	..	+ (1)	Sens.	–	Mild	Good
9	M	1 8/12	3 Rel.*	400 × 2 840 × 7†	(Table II)	(Table II)	(Table II)	+ (6) + (3)	<1 μ. per ml. > 400 μ per ml.	+ +	Sev.	Died
10	M	1 11/12	4	600 × 10	50 × 10	8–16	..	–	..	+	Mild	Good
11	M	2	20 Rel.	500 × 10 500 × 13	50 × 10 50 × 10	8–16 16	33 55	+ (1) + (1)	22 mm. Sens.	+ Not done	Mod.	Good
12	M	2 9/12	3	1000 × 1	150 × 1	2	..	+	<1 μ per ml.	–	Sev.	Died

Rel. = relapse. Con. = contaminated. * Relapse treated with sulphamezathine and penicillin (these drugs were also given with the streptomycin in the primary attack). † Including day of admission. ‡ Treated with combined therapy.

Digitized by Google

organism remained sensitive. In a fourth (case 9) the organism persisted in the C.S.F., and daily estimations showed a rapid diminution of sensitivity. Originally the strain was inhibited by 1 unit of streptomycin, but forty-eight hours later it grew in 400 units. At necropsy four weeks later it was still insensitive.

Results.—Of 8 patients treated with streptomycin alone 2 died and 6 recovered. Of 3 patients treated with combined therapy 1 died. Case 2 is excluded because no organism was grown from the C.S.F. or from the blood before streptomycin was given. Thus of 11 patients 3 died, giving a case-mortality of 27%. The C.S.F. became sterile within twenty-four hours of the start of streptomycin treatment in 7 cases out of 9.

CASE-RECORDS

On admission, besides a complete physical examination, every child underwent the following investigations as a routine: lumbar puncture, throat swab, blood-count, examination of urine, blood-culture, and radiography of chest. Positive findings alone are recorded. The C.S.F. was examined daily. The number of days during which *H. influenzæ* was cultured after the start of streptomycin treatment is noted in parentheses. This includes the one C.S.F. culture made from material taken immediately before the start of streptomycin treatment. The organism grown from C.S.F. was typed in every case and found to be Pittman's type B.

Case 1.—A boy, aged 9 months, had become irritable in the morning of March 12, 1947, vomited at midday, and then had a convulsion lasting an hour. For the next ten days he had been quiet and rather listless. He had been admitted to hospital on March 22 with well-marked neck rigidity. Lumbar puncture (March 26) produced turbid C.S.F. which on culture grew *H. influenzæ*. Penicillin 200,000 units intramuscularly three-hourly and sulphathiazole 1 g. four-hourly had been given from March 22 to 28 and then discontinued because the temperature had been normal for three days. The patient had relapsed in the evening of March 28, and was transferred to the London Hospital on March 30.

On Admission.—Temperature 101°F, pulse-rate 140 per min. He did not look very ill. He followed objects with his eyes and grasped with his hands. There was well-marked head retraction and neck rigidity. The fontanelle was not tense. Pus was aspirated from an abscess in the thigh (? site of penicillin injections) and was sterile on culture. C.S.F. purulent; pressure 120 mm. H_2O; protein 600 mg. per 100 ml.; culture grew *H. influenzæ* (1), growth inhibited on Fildes's agar containing 2 units of streptomycin per ml. Hæmoglobin 58%, white cells 23,000 per c.mm. (polymorphs 48%).

Treatment.—Streptomycin intramuscularly 500 mg. daily from March 30 to April 8, and intrathecally 25 mg. daily from March 31 to April 7. The first three injections were intraventricular, because the C.S.F. flowed with difficulty on lumbar puncture. The C.S.F.-streptomycin level had an average range of 4–8 units per ml.

Progress.—The patient had continuous pyrexia over 100°F throughout the illness, with frequent vomiting. *April 2 and 3:* ventricular C.S.F. contained many pus cells and protein 1500 mg. per 100 ml.; culture proved sterile. *April 9:* gastro-enteritis. *April 12:* bilateral mastoid antrotomy; no pus found; swabs sterile. *April 14:* convulsion. *April 20:* passed a formed stool and seemed to be improving, but in the evening had a convulsion, with clonic movements and spasticity of the right side. *April 21:* grey and critically ill; right-sided fits continued; an operation was performed to exclude localised intracranial pus, and no pus was found; C.S.F. contained 25 cells per c.mm., and protein 50 mg. per 100 ml.; culture proved sterile. *April 22:* the patient died.

Necropsy Findings.—Fibrous matting of leptomeninges at the base of the brain; a ragged cavity 2 cm. in diameter in the left frontal lobe, containing fragments of blood-clot, lined by soft ragged sloughing tissue and communicating with the left lateral ventricle; moderate dilatation of all ventricles; extremely fatty liver. Microscopically there was no evidence of active meningitis over the brain or cord, and no inflammatory reaction in the wall of the cavity in the left frontal lobe.

This was a moderately severe case which was controlled by streptomycin but subsequently developed gastro-enteritis. The cause of the cavity in the frontal lobe remains obscure. A possible explanation is that some streptomycin was injected at this site.

Case 2.—A boy, aged 9 months, had begun to be feverish on May 2, 1947, followed two days later by a fit, with twitching of the right side of the body, staring eyes, and protrusion and retraction of the tongue. Subsequently, whenever the child cried, his right hand had twitched. On May 13 he had been admitted to hospital, with temperature 104°F, pulse-rate 140, respirations 36 per min., and neck rigidity. The fontanelle had not been tense. C.S.F. had been purulent and contained gram-negative organisms resembling *H. influenzæ*. The patient had been given 'Sulphamezathine' from May 14 to 31 a total of 24 g.; and penicillin 25,000 units intrathecally daily from May 16 to 26; 50,000 units intrathecally on alternate days from May 26 to June 2; and 6000 units by mouth three-hourly from May 14 to June 2. During this period there had been a persistent fever and steady deterioration in his clinical condition. On May 31, *H. influenzæ* had still been present in the C.S.F., and on June 2 the patient was transferred to the London Hospital.

On Admission.—Temperature 101°F, pulse-rate 140 per min., well-marked head retraction and opisthotonos; fingers clenched over thumbs; legs hyperextended. The patient appeared mentally impaired. The fundi showed moderate pallor of both discs. The fontanelle was not tense. Neck rigidity and generalised spasticity, with tremor of the arms and ankle clonus, were present. The abdominal reflexes were absent, and all tendon-reflexes exaggerated. White-cell count 17,000 per c.mm. (polymorphs 70%). C.S.F.: pressure 150 mm. H_2O; 345 cells per c.mm.; protein 110 mg. and sugar 35 mg. per 100 ml.; culture sterile. Blood-culture also proved sterile.

Treatment.—Streptomycin 600 mg. intramuscularly daily and 100 mg. intrathecally daily from June 2 to 8.

Progress.—The patient was afebrile after three days. C.S.F. (June 8) 120 cells per c.mm. and protein 100 mg. per 100 ml.; it subsequently became normal. Streptomycin level in C.S.F. 32–64 units per ml. There was no improvement in the neurological condition, though general progress was satisfactory, and when discharged (Aug. 8, 1947) the patient was mentally defective, blind with optic atrophy, and had generalised spasticity. On Aug. 8, 1948, the patient was still alive, and his condition unchanged.

This was a subacute case deteriorating while on penicillin and sulphamezathine, though the infection may have been controlled. The C.S.F. was sterile on culture when streptomycin therapy was begun.

Case 3.—A girl, aged 9 months, had fallen from her perambulator on April 1, 1947, but had not lost consciousness. On April 21 she had been feverish, vomited repeatedly, and been admitted to hospital with neck rigidity and turbid C.S.F., which grew *H. influenzæ* on culture. She had been given sulphonamides 3 g. daily for nine days, and penicillin 20,000 units intramuscularly four-hourly for four days and 10,000 units intrathecally once. On May 8 her condition had remained unchanged, and her C.S.F. contained 300 cells per c.mm. and protein 100 mg. per 100 ml. and grew *H. influenzæ* on culture. On May 13 the patient was transferred to the London Hospital.

On admission the patient appeared pale and moderately ill, with head retracted and neck rigid, temperature 102°F, pulse-rate 180 per min., right pupil dilated with no reaction to light. A blood-culture was contaminated. White-cell count 12,200 per c.mm. (polymorphs 84%) C.S.F. contained 650 cells per c.mm., protein 140 mg. and sugar 30 mg. per 100 ml., and on culture grew *H. influenzæ* (3), sensitive to a ring 21 mm. in diameter.

Treatment.—Streptomycin 480 mg. intramuscularly daily from May 13 to June 9, 50 mg. intrathecally daily from May 13 to 15, and 25 mg. intrathecally daily from May 16 to 26; penicillin 120,000 units intramuscularly daily from May 22 to June 15, 5000 units intrathecally daily from May 22 to 26; sulphamezathine 3 g. daily from May 22 to June 15. The C.S.F.-streptomycin level was 16–32 units per ml.

Progress.—The patient became afebrile on May 15 and clinically improved by May 21. May 26: C.S.F. contained 8000 red cells and 140 white cells per c.mm., and protein

Digitized by Google

60 mg. per 100 ml. On May 29 the pupils were normal. On June 7 there was no neck rigidity and the patient was playing normally. When last seen, on July 28, 1948, she appeared to be normal.

This was a moderately severe case probably cured with streptomycin. The course of treatment was prolonged and combined therapy was instituted, because a gram-negative bacillus was persistently found in the stained deposit of the C.S.F., though the culture was sterile. This organism subsequently proved to be a stain contaminant.

Case 4.—A girl, aged 1 year, had become feverish and unwell on Dec. 20, 1947, and had been admitted to hospital on Dec. 23, with temperature 100·6°F, pulse-rate 160, respirations 20 per min., injected fauces, and neck rigidity. The C.S.F. had contained 480 cells per c.mm. and protein 250 mg. per 100 ml., and on culture had grown *H. influenzæ*. She had been given sulphadiazine 1·5 g. daily for seven days and penicillin 20,000 units three-hourly intramuscularly for two days, 100,000 units three-hourly for another two days, and 20,000 units intrathecally twice.

On Dec. 30 she was transferred to the London Hospital, with temperature 101°F, pulse-rate 160 and respirations 46 per min., throat injected, nasal catarrh, well-marked neck rigidity. A throat swab and a blood-culture showed *H. influenzæ* present. Hb 58%, white-cell count 16,400 per c.mm. (polymorphs 56%). C.S.F. contained 600 cells per c.mm. and protein 50 mg. per 100 ml., and on culture grew *H. influenzæ* (1) sensitive to streptomycin.

Treatment.—Streptomycin 400 mg. intramuscularly daily and 50 mg. intrathecally daily from Dec. 30, 1947, to Jan. 6, 1948. The average range of the C.S.F.-streptomycin level was 2–4 units per ml.

Progress.—On Dec. 31, 1947, there was a remarkable improvement, the patient crawling about her cot. She had slight neck rigidity, was afebrile after four days, and made an uneventful recovery. On Jan. 7, 1948, the C.S.F. contained 16 lymphocytes per c.mm. and protein 120 mg. per 100 ml. A follow-up examination in August, 1948, showed her to be normal.

This was a moderately severe early case which recovered after a single course of streptomycin.

Case 5.—A girl, aged 1 year, had been vomiting and irritable, but without convulsions, on Feb. 1, 1948. On Feb. 5 she had been unable to move her legs, and had been given sulphamerazine to a total dosage of 2·25 g. On Feb. 8 she had been admitted to hospital with her C.S.F. containing 5500 cells per c.mm. and gram-negative bacilli. She had been given sulphathiazole 1·5 g. On Feb. 9 she had been transferred to the London Hospital, with temperature 101°F, pulse-rate 150 and respirations 40 per min. She did not appear very ill and was mentally alert. She had slight neck rigidity, swelling of the right leg, especially over the ankle-joint; limitation of movement of the left hip, with swelling in the inguinal region; and pitting œdema of both feet. A throat swab and blood-culture both showed *H. influenzæ* present. Hb 67%, white-cell count 25,000 per c.mm. (polymorphs 50%). Radiography of chest, pelvis, and ankle showed no abnormality. Lumbar puncture produced purulent C.S.F. containing protein 80 mg. and sugar 30 mg. per 100 ml. Culture produced *H. influenzæ* (1), sensitive to a ring 15 mm. in diameter.

Treatment.—Streptomycin 500 mg. intramuscularly daily from Feb. 9 to 23, and 50 mg. intrathecally daily from Feb. 9 to 19. Both legs were immobilised in extension. The average C.S.F.-streptomycin level was 8 units per ml.

Progress.—On Feb. 10, aspiration of the right ankle-joint produced a few drops of very thick pus containing gram-negative bacteria. A culture proved sterile. By Feb. 18 there was steady slow improvement, the patient being afebrile and having no neck rigidity. On Feb. 25 there was an abscess of the left thigh at the site of an intramuscular injection. *Staph. pyogenes* was grown from the pus. The C.S.F. was repeatedly sterile. On Feb. 19 the C.S.F. contained 41 cells per c.mm., protein 50 mg. and sugar 57 mg. per 100 ml. Otherwise recovery was uneventful, and at follow-up in August the child was normal.

This was a moderately severe case, with purulent arthritis of the left hip and right ankle, which recovered after a single course of streptomycin.

Case 6.—A girl, aged 1 year, had developed nasal catarrh and become drowsy and listless on Dec. 16, 1947, and had been admitted to hospital on Dec. 21 with left basal pneumonia. She had been given sulphamezathine, to a total dosage of 16 g. Her temperature had subsided at first but had risen again on Dec. 25. Chemotherapy had been discontinued on Dec. 26. On Dec. 27 she had had neck rigidity. From Dec. 28 penicillin 30,000 units four-hourly to a total of 520,000 units was given intramuscularly. On Dec. 29 her C.S.F. had contained 279 cells per c.mm. and protein 40 mg. per 100 ml., and on culture had produced *H. influenzæ*. She had then been given sulphadiazine 3 g. On Dec. 31 she was transferred to the London Hospital.

On admission her temperature was 103°F, pulse-rate 140 and respirations 30 per min. She was drowsy, with some clouding of consciousness, but was easily roused. Both ear drums were injected. The liver and spleen were just palpable. Neck rigidity was well marked. Abdominal reflexes were absent. Hb 60%, white-cell count 20,500 per c.mm. (polymorphs 48%). Blood-culture gave *H. influenzæ*, sensitive to a ring 23 mm. in diameter. C.S.F. contained 245 cells per c.mm. and protein 40 mg. per 100 ml., and on culture grew *H. influenzæ* (1).

Treatment.—Streptomycin 400 mg. intramuscularly daily and 50 mg. intrathecally daily from Dec. 31 to Jan. 8, 1948. The C.S.F.-streptomycin level was 8 units per ml.

Progress.—There was steady clinical improvement, but fever (100–102°F) persisted until Jan. 7, 1948, after which it fell to 99°F. On Jan. 8 the C.S.F. contained 60 cells per c.mm. and protein 90 mg. per 100 ml. Neck rigidity was still present on Jan. 10. On Jan. 12 the temperature was 103°F and the patient was restless and fretful, with more neck rigidity. C.S.F. contained 580 cells per c.mm. and protein 70 mg. per 100 ml., and on culture grew *H. influenzæ* (1), sensitive to a ring 15 mm. in diameter. Blood-culture proved sterile.

Further Treatment.—Streptomycin 400 mg. intramuscularly daily from Jan. 12 to 22, 100 mg. intrathecally daily from Jan. 12 to 16, and 50 mg. intrathecally daily from Jan. 17 to 22. The C.S.F.-streptomycin level was 32–64 units per ml.

Further Progress.—Steady improvement followed, temperature falling to 99°F by next day and remaining at this level, except for occasional spikes to 100°F, until Jan. 23, when it returned to normal. On Jan. 22 there was no neck rigidity, and the C.S.F. contained 72 cells per c.mm. and protein 120 mg. per 100 ml. The patient made an uneventful recovery, and at follow-up in August, 1948, appeared normal.

This was a moderately severe case, which relapsed after a full course of streptomycin, but recovered after a second course.

Case 7.—A girl, aged 1 year, had vomited, shivered, and for a time could not be roused, on April 18, 1948. On April 20 she had been admitted to hospital very ill and dyspnœic, and diagnosed as acute follicular tonsillitis and bronchopneumonia. She had been given penicillin 10,000 units intramuscularly six-hourly from April 20 to 25; sulphonamides total dosage 10 g. from April 20 to 27. A radiogram of her chest had shown nothing abnormal. She had remained febrile, but her condition had improved. On April 30 she had relapsed, with slight neck rigidity. Lumbar puncture had produced turbid C.S.F., and a stained film of the deposit showed organisms resembling *H. influenzæ*. The patient was thereupon transferred to the London Hospital.

On Admission.—Temperature 98°F, pulse-rate 100 and respirations 34 per min. She looked ill and grey, crying monotonously when roused, but rapidly sinking back into a semicomatose state, grinding her teeth, and with muscular twitchings of the face. Neck rigidity was well marked. The ear drums were injected. Hb 70%, white-cell count 37,800 per c.mm. (polymorphs 73%). Blood-culture produced *H. influenzæ*. C.S.F. contained 1280 cells per c.mm., protein 120 mg. and sugar 20 mg. per 100 ml., and on culture produced *H. influenzæ* (1) sensitive to streptomycin.

Treatment.—Streptomycin 500 mg. intramuscularly daily from April 30 to May 10, and 50 mg. intrathecally daily from April 30 to May 9. The C.S.F.-streptomycin level had an average range of 8–16 units per ml.

Progress.—On May 10 there was little if any clinical improvement (for temperature see fig. 1). Streptomycin was discontinued after the C.S.F. had been sterile for nine days. On May 11 a few crepitations were heard at the

Digitized by Google

left base, and the patient was given sulphadiazine 1·5 g. daily for six days in view of the possible development of pneumonia. The C.S.F. contained 52 cells per c.mm., protein 40 mg. and sugar 50 mg. per 100 ml., and on culture proved sterile. On May 14 there was a sudden rise in temperature, and the C.S.F. contained 295 cells per c.mm., protein 40 mg., and sugar 30 mg. per 100 ml., and culture gave *H. influenzæ* (1). Blood-culture was sterile.

Further Treatment.—Streptomycin 500 mg. intramuscularly daily and 50 mg. intrathecally daily from May 13 to 19. The C.S.F.-streptomycin level was 8 units per ml.

Further Progress.—Some improvement followed. The patient was smiling and taking more interest. On May 19 there was no neck rigidity and no pyrexia. On May 21 there was pyrexia in the evening, and the C.S.F. contained 37 cells per c.mm., and protein 35 mg. per 100 ml., but culture proved sterile. On May 22 the C.S.F. contained 19,000 cells per c.mm., protein 120 mg. and sugar 32 mg. per 100 ml., and on culture produced *H. influenzæ* (3), sensitive to a ring 15 mm. in diameter. Blood-culture also proved positive.

Further Treatment.—Streptomycin 500 mg. intramuscularly daily from May 22 to June 2, and 50 mg. intrathecally daily from May 22 to June 1. On May 22 specific type-B *H. influenzæ* rabbit antiserum 50,000 units was given intravenously.

Further Progress.—Bilateral myringotomy was done on May 28, but no pus was found. On May 31 the patient was pulling herself up and playing. Lumbar puncture became increasingly difficult. The C.S.F. tended to be bloodstained and showed a rise in protein content to 200 mg. per 100 ml. on May 29. The possibility of a spinal block developing was considered, but in view of her clinical improvement it was decided to treat her conservatively, and streptomycin was discontinued. On June 3 the patient had an urticarial eruption; otherwise recovery was uneventful (see fig. 1), and at follow-up in August, she was normal.

This patient was severely ill, with drowsiness and protracted semicoma suggesting encephalitis. She relapsed twice after two full courses of streptomycin, but recovered after a third course combined with type-B *H. influenzæ* antiserum.

Case 8.—A boy, aged 16 months, whose sister had died in 1937 of *H. influenzæ* meningitis at the age of 13 months, had been visited on Dec. 13, 1947, in a day nursery by his father, who had noted that he was thin and pale, "had a vacant look," and gave no sign of recognition. On Dec. 17 the child had been admitted to hospital with neck rigidity. A lumbar puncture had produced turbid C.S.F. containing gram-negative bacilli, but sterile on culture. He had been given sulphamezathine 4 g. and sulphadiazine 1·5 g. On Dec. 18 he was transferred to the London Hospital.

On Admission.—Temperature 101°F, pulse-rate 136 and respirations 36 per min. The patient lay quietly but was easily roused. Neck rigidity was present. There was slight swelling of the right arm, which showed an increase of ½ in. in circumference around the elbow. Hb 71%, white-cell count 17,600 per c.mm. (polymorphs 57%). C.S.F. contained 12,700 cells per c.mm., and protein 40 mg. per 100 ml., and on culture gave *H. influenzæ* (1).

Treatment.—Streptomycin 500 mg. intramuscularly daily and 50 mg. intrathecally daily from Dec. 19 to 27. The C.S.F.-streptomycin level was 2–8 units per ml.

Progress.—On Dec. 22 there was clinical improvement and no neck rigidity. On Dec. 23 the patient was afebrile. On Dec. 27 his right arm was no longer swollen, and his C.S.F. contained 60 cells per c.mm. and protein 50 mg. per 100 ml. At a follow-up in August, 1948, the patient was very well, except that he seemed slightly deaf. He had not yet begun to talk.

This was a mild case, with arthritis of the right elbow, which responded well to streptomycin.

Case 9.—A boy, aged 17 months, had frequent attacks of projectile vomiting and became listless on April 23, 1947. Next day he was semiconcious and was taken to hospital, where lumbar puncture had produced turbid C.S.F. which on culture grew *H. influenzæ*. On April 26 the patient was transferred to the London Hospital.

On Admission.—Temperature 102°F, pulse-rate 160 and respirations 32 per min. The patient was drowsy, ill, and grey, but coöperative. The spleen was palpable. There was moderate neck rigidity. A blood-culture was positive. Hb 65%, white-cell count 19,000 per c.mm. (polymorphs 48%). C.S.F. contained 6000 cells per c.mm. and protein 120 mg. per 100 ml., and on culture grew *H. influenzæ*.

Treatment.—Streptomycin 400 mg. intramuscularly daily from April 26 to 28, 840 mg. intramuscularly daily from April 29 to May 5, and 75–200 mg. intrathecally daily from April 26 to May 1; penicillin 50,000 units intramuscularly four-hourly from April 30 to May 14; and sulphamezathine 4·5 g. daily from May 2 to 5, and 3 g. daily from May 6 to 14 (see table II).

Progress.—On April 28 the intrathecal dosage of streptomycin was increased because the C.S.F.-streptomycin level remained low. On April 29 the patient was found to have arthritis involving the right knee, right elbow, left wrist, and the interphalangeal joints of both big toes; 20 ml. of pus was aspirated from the knee, and on culture it grew *H. influenzæ*. Streptomycin 25 mg. was injected into the knee-joint and into the left wrist. The legs were immobilised in extension. On April 30, because *H. influenzæ* was still being cultured from the C.S.F., intramuscular penicillin therapy was started. On May 2 the patient was deteriorating, and intrathecal streptomycin was discontinued because the infecting organism had become resistant. Sulphamezathine therapy was started. On May 10 the patient was much improved, playing with toys, but still febrile. Pus from the knee was sterile. On May 14, the C.S.F. having been sterile for twelve days and containing 3 cells per c.mm. and protein 20 mg. per 100 ml., chemotherapy was stopped. On May 16 the patient had a relapse, with vomiting and fretfulness, but no definite neck rigidity. A blood-culture was positive. The C.S.F. contained 3000 cells per c.mm. and protein 50 mg. per 100 ml., and on culture grew *H. influenzæ* (2) insensitive to streptomycin but slightly sensitive to penicillin.

Further Treatment.—Sulphamezathine 3 g. daily; penicillin 50,000 units intramuscularly four-hourly from May 16 to 28, 10,000 units intrathecally daily for three days, and 5000 units intrathecally daily for eight days from May 18 to 28.

Further Progress.—On May 21 the C.S.F. contained 40 cells per c.mm. and protein 40 mg. per 100 ml. There was continuous fever over 100°F, but the patient began to improve

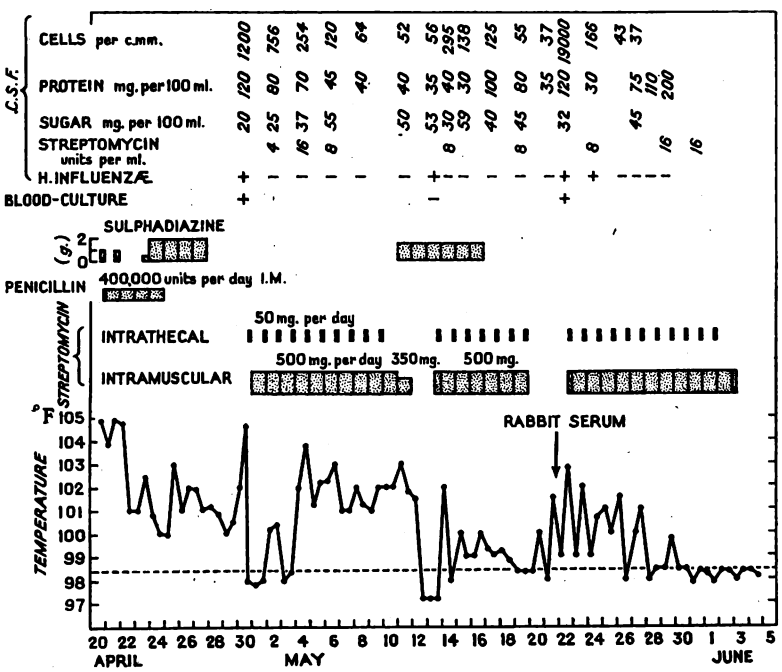


Fig. 1—Chart of severe case, showing two relapses after treatment with streptomycin (case 7).

Digitized by Google

TABLE II—*H. influenzæ* MENINGITIS INSENSITIVE TO INCREASING DOSES OF STREPTOMYCIN BUT RESPONDING TO COMBINED THERAPY (CASE 9).

Date (1947)	Intramuscular streptomycin (mg.)	Intrathecal streptomycin (mg.)	Cerebrospinal fluid: Streptomycin level (u./ml.)	Cerebrospinal fluid: Cells per c.mm.	Cerebrospinal fluid: Protein (mg./100 ml.)	Cerebrospinal fluid: Sugar (mg./100 ml.)	Cerebrospinal fluid: *H. influenzæ*	Intramuscular penicillin (units)	Sulphamezathine (g.)
April 27: 2 A.M.	400	50	..	6000	120	..	+*	..	..
10 A.M.		25	1	26,000	50	..	+	..	..
April 28: A.M.	400	25	1	13,000	50	53	+	..	..
P.M.		75	2	1000	30	64	+	..	..
April 29: A.M.	840	65	4	400	40	72	+†	..	..
P.M.		50	..	..	..	..	..	..	..
April 30: A.M.	840	100	2	7000	140	..	+	300,000	..
May 1: A.M.	840	100	8	3680	20	53	+	300,000	..
P.M.		100	16	1700	..	..	+	..	..
May 2	840	..	4	Pus	50	60	+	300,000	4·5
May 3	840	..	..	..	..	..	..	300,000	4·5
May 4	840	..	8	208	30	..	−	300,000	4·5

* Sensitive to 1 unit but grew in 1/5 unit streptomycin per ml.
† Insensitive to 400 units streptomycin per ml.

clinically. On May 25 he developed measles, and on May 27 suppurative laryngitis for which he underwent tracheotomy; but he died the same day. The C.S.F. had been sterile for nine days before death.

Necropsy Findings.—Many small patches of fibrinopurulent exudate on the cerebral hemispheres produced, on culture, *H. influenzæ* insensitive to streptomycin. A very recent antemortem thrombus in the superior longitudinal sinus. Mucopus in ethmoid air-cells, nasal cavity, and maxillary antra. Greyish-yellow mucopurulent membrane lining the larynx above the true vocal cords excluding the epiglottis, and giving on culture *Staph. pyogenes* and *Bact. coli*. Mottled dark-red areas of pneumonia throughout the lungs. No abnormality in the right knee-joint.

This was a case of severe infection, with multiple arthritis. The infecting organism became rapidly insensitive to streptomycin despite big doses. Increasingly large intrathecal doses were used when the C.S.F.-streptomycin level (repeatedly estimated) remained low. Penicillin and sulphonamides subsequently sterilised the C.S.F., but death followed measles with suppurative laryngitis. Necropsy showed that pus on the cerebral hemispheres still contained *H. influenzæ*.

Case 10.—A boy, aged 1 year 11 months, had had fever and anorexia on Jan. 2, 1948, and pneumonia had been diagnosed. He had been admitted to hospital on Jan. 4, with neck rigidity. His C.S.F. had contained 1000 cells per c.mm., protein 40 mg. and sugar 60 mg. per 100 ml., and, on culture, had grown *H. influenzæ*. The patient had been given sulphadiazine to a total of 7·5 g. and penicillin 60,000 units intramuscularly four-hourly until he was transferred to the London Hospital on Jan. 6.

On Admission.—Temperature 100°F, pulse-rate 130 and respirations 24 per min. The patient was drowsy but conscious, with well-marked neck rigidity. A blood-culture grew *H. influenzæ*. The C.S.F. contained 334 cells per c.mm. and protein 100 mg. per 100 ml. Culture proved sterile.

Treatment.—Streptomycin 600 mg. intramuscularly daily and 50 mg. intrathecally daily from Jan. 6 to 15. The C.S.F.-streptomycin level was 8–16 units per ml.

Progress.—There was steady improvement to complete recovery. By Jan. 13 there was no neck rigidity and the patient was afebrile. On Jan. 15 the C.S.F. contained 48 cells per c.mm. and protein 80 mg. per 100 ml. At follow-up in August he was normal.

This was a mild case, in which the C.S.F. was sterile after penicillin and sulphadiazine, but blood-culture was still positive before streptomycin treatment.

Case 11.—A boy, aged 2 years, had vomited several times and become feverish and weak on his legs on May 4, 1948. Next day he had been admitted to hospital with temperature 101°F, pulse-rate 120 and respirations 25 per min., and looking pale, ill, and slightly cyanosed, with doubttul signs in the chest and doubtful neck rigidity. Bronchopneumonia had been diagnosed and treated with penicillin 20,000 units three-hourly and sulphamezathine 0·5 g. six-hourly. Temperature had fallen during the first five days but risen again on May 10 within a day of stopping treatment. On May 17 lumbar puncture had produced C.S.F. under pressure of 300 mm. H_2O, containing 1000 cells per c.mm. and protein 45 mg. per 100 ml. Penicillin 10,000 units intrathecally daily and 20,000 units three-hourly intramuscularly had been given for three days without improvement. On May 23 the infecting organism had been identified as *H. influenzæ*. On May 24 the patient was transferred to the London Hospital.

On Admission.—Temperature 100°F. Moderate neck rigidity. Blood-culture grew *H. influenzæ*. White-cell count 25,000 per c.mm. (polymorphs 75%). C.S.F. contained 960 cells per c.mm., protein 60 mg. and sugar 57 mg. per 100 ml., and on culture grew *H. influenzæ* (1), sensitive to a ring 22 mm. in diameter.

Treatment.—Streptomycin 500 mg. intramuscularly and 50 mg. intrathecally daily from May 24 to June 2. The C.S.F.-streptomycin level was 8–16 units per ml.

Progress.—On May 26 the patient became afebrile and began a rapid clinical improvement (fig. 2). On May 28 there was no neck rigidity, and he was playing. On June 1 the C.S.F. contained 12 cells per c.mm., protein 50 mg. and sugar 51 mg. per 100 ml. On June 5 the patient's temperature was 101°F, and he was fretful and crying, with watery nasal discharge, injected fauces, and neck rigidity. The C.S.F. contained 610 cells per c.mm., protein 200 mg. per 100 ml., and on culture grew *H. influenzæ* (1).

Further Treatment.—Streptomycin 500 mg. intramuscularly daily from June 5 to 17, and 50 mg. intrathecally from June 5 to 14. The C.S.F.-streptomycin level was 16 units per ml.

Further Progress.—Clinical improvement was noted on June 9, on June 12 there was no neck rigidity, and on June 13 the patient was afebrile. He made an uneventful recovery (see fig. 2), and at follow-up in August he was normal.

This was a moderately severe case which relapsed after apparent recovery and was cured by a second course of streptomycin.

Case 12.—A boy, aged 2 years 9 months, had developed anorexia, vomiting, increasing restlessness, and drowsiness on April 5, 1947, and frontal headache on April 7. At 10 P.M. on April 8 he was admitted to the London Hospital.

On Admission.—Temperature 102°F, pulse-rate 160 and respirations 22 per min. The patient was very ill and faintly cyanosed, lying with his eyes half-closed and head retracted. His fauces were injected. No abnormality was detected in the respiratory system. He was semicomatose, reacting to pin-prick but not to spoken commands. Neck rigidity was severe; flexion caused piercing screams. There was generalised hypotonia, with abdominal reflexes absent. The left plantar response was flexor, and the right extensor. Blood-

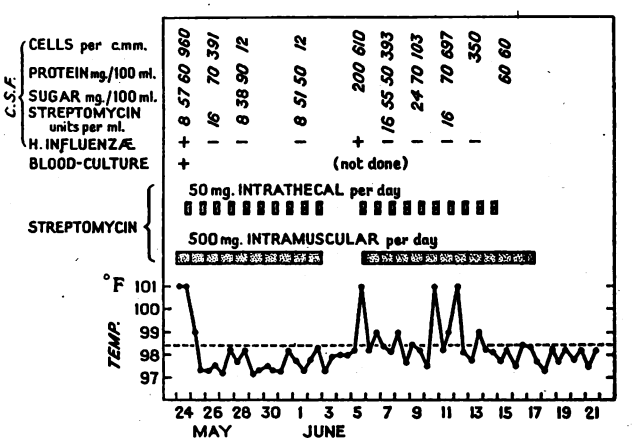


Fig. 2—Chart of mild case, showing apparently satisfactory response to streptomycin followed by relapse (case 11).

Digitized by Google

culture proved sterile. The C.S.F., under a pressure of 300 mm. H_2O, contained 17,000 cells per c.mm., and grew *H. influenzæ* on culture.

Treatment and Progress.—Streptomycin 1/6 g. intramuscularly four-hourly, and 50 mg. intrathecally immediately. Twelve hours later (April 9) there was an abrupt onset of choking, with bubbling noises in the pharynx; this cleared after half an hour. Temperature 104°F, pulse-rate 160 per min. The patient was critically ill, and his colour ashen grey. Signs of consolidation in the left upper lobe were confirmed by radiography. Lumbar puncture was done at 6 P.M. and streptomycin 100 mg. was given intrathecally. The C.S.F.-streptomycin level was 2 units per ml. Gram-negative coccobacilli were present in a film of C.S.F. The patient died at 11 P.M.

Necropsy Findings.—Purulent meningitis; ill-defined areas of peribronchial consolidation in the lungs; stomach contents and greenish-yellow mucus filling trachea and bronchi. In a smear from meningeal pus gram-negative organisms were seen, but a culture was contaminated. Ventricular fluid contained gram-negative organisms. Culture from the lungs gave *Staph. pyogenes*.

This was a fulminating infection with meningitis and pneumonia, and the patient died twenty-five hours after streptomycin therapy had been started.

DISCUSSION

Though probably less common in this country than in the United States (Mutch 1941), *H. influenzæ* infection is an important cause of suppurative meningitis, particularly in children under the age of 2 years. In the present series 12 cases were admitted in fifteen months. All were transferred, however, from hospitals covering a wide area. A more normal rate of admission is indicated by a review of 10 cases admitted to the London Hospital in 1927–36 (Williams and Tallerman 1937).

No attempt is made to describe the clinical picture in detail, but a few points are emphasised that may help in early diagnosis, since this is essential if good results are to be achieved.

The diagnosis is most difficult in young infants, the age at which the prognosis is worst (Alexander 1943). Not infrequently a mild upper respiratory infection precedes an abrupt febrile onset of vomiting, irritability, convulsions, or drowsiness. Physical signs may be absent in the early stages. Increased tension of the fontanelle generally appears earlier than neck rigidity. Slight disturbances of consciousness may develop, often no more than a vacant glazed look about the eyes. In the presence of any of these physical signs, or in an unexplained pyrexia associated with any of the above-mentioned symptoms, it is essential to perform lumbar puncture. The diagnosis is then confirmed or refuted, and, if an infection is present, the type of organism can be determined.

In older children headache, vomiting, and neck rigidity are generally well marked, and the diagnosis correspondingly less difficult. All variations in the severity of the disease occur, from a fulminating type, which may even present with the Waterhouse-Friderichsen syndrome (Lindsay et al. 1940), to a subacute insidious form resembling tuberculous meningitis.

In the present cases the usual high incidence of septicæmia was found, 7 out of 9 blood-cultures being positive on admission. Arthritis developed in 3 out of 12 cases, in 2 involving more than one joint. In 4 cases the original diagnosis was pneumonia. It is important to realise that meningitis may be masked by a pneumonic mode of presentation. In some instances *H. influenzæ* pneumonia may actually precede (Huntington and Weiss 1936) or accompany the onset of meningitis, and meningitic signs may be attributed to "meningism." In other cases pneumonia may be simulated by the presence of rapid grunting respirations and by the deceptive fall in temperature and clinical improvement that may follow treatment with sulphonamides. It is unjustifiable to maintain this diagnosis in the continued absence of physical signs in the chest or of radiographic confirmation, unless meningitis has been excluded by lumbar puncture.

Some assessment of the severity of a case is required as a guide in treatment. Two types of severe case occur, one a short fulminating illness, the other a subacute form that has deteriorated into a critical state. Generally the following features (largely derived from Alexander's work) indicate that the disease is likely to run a severe course.

(1) An age of less than seven months.
(2) A rapid downhill course, with the early appearance of coma or of multiple fits.
(3) Deep and protracted coma suggesting encephalitis.
(4) Complications, especially laryngotracheo-bronchitis, pneumonia, or multiple suppurative arthritis.
(5) Lack of response to treatment, shown by a persistently high temperature, no clinical improvement, the persistence of organisms in the C.S.F., or the development of resistance to the drug.

It has also been stated (Alexander 1944) that a C.S.F.-sugar level of less than 15 mg. per 100 ml. indicates a severe infection. The sugar concentration was estimated in 6 of these cases, including 2 clinically severe ones, and it exceeded this level in all of them.

Alexander et al. (1946) have stated that, though streptomycin is effective in controlling mild or moderately severe cases, it often fails in the more severe infections. In the present small series our results point to a similar conclusion.

Of 3 cases classified as severe on clinical grounds one ran a rapid downhill course, the second developed multiple pyarthroses and a resistant strain of organism, and the third ran a continuous fever and remained in a semicomatose state for nine days and subsequently relapsed twice. All these children looked ill and had a dusky grey complexion in contrast to the milder cases, who generally looked fairly well. Of the 7 moderately severe cases 6 completely recovered. The one child who died also had gastro-enteritis and at necropsy showed no evidence of active disease.

Streptomycin compares favourably with combined treatment with specific antiserum and sulphonamides, but neither form of therapy alone gives satisfactory results in severe cases. For these Alexander et. al (1946) considered that treatment with all three agents would prove most effective and the treatment of choice. Though penicillin combined with sulphonamides does not appear to be so effective as streptomycin it may yet prove useful in combined therapy.

Relapses

In 3 cases there was a relapse after streptomycin treatment, 1 of these had two relapses. Such a high proportion of relapses has not previously been reported with streptomycin. The initial course of treatment lasted eight days in 1 case and ten days in the other 2, and a second course of eight days was given to the case that relapsed twice. The C.S.F. became sterile within twenty-four hours in each case. No definite indications of the likelihood of a relapse were found, except that it was more liable to occur in severe infections and when fever persisted. Case 11, however, relapsed after being afebrile for ten days; he had been sitting up and playing, and the C.S.F. had returned almost to normal. One significant feature in these cases was the duration of illness before streptomycin therapy was started. It was ten, fifteen, and twenty days, whereas in those that recovered on a single course it was four, five, eight, and ten days. Of Alexander's 12 patients, most of whom received a shorter course of treatment without a relapse, none had been ill longer than seven days (Alexander et al. 1946).

The necropsy in case 9 indicated a possible source of a relapse. The infecting organism in this case became resistant to streptomycin but responded to penicillin

Digitized by Google

and sulphonamides. Subsequently there was a relapse which was controlled by the same treatment. Death was due to a complicating suppurative laryngitis when the C.S.F. had been sterile for nine days, and there was clinical evidence of improvement of the meningitis. Necropsy showed scattered areas of pus over the cerebral hemispheres from which *H. influenzæ* was grown. Such foci might well be responsible for relapses. Presumably in other cases such residual foci may be situated in the lungs, joints, middle ears, or sinuses, and may be the origin of a relapse with septicæmia and meningitis. Perhaps more attention should be directed to the sinuses, which may be involved in the initial infection of the upper respiratory tract. Field and Rogers (1936) reported a case of meningitis which they considered secondary to an infected sphenoidal sinus from which *H. influenzæ* was grown post mortem. Mucopus was found in the maxillary and ethmoid antra at necropsy in case 9; unfortunately it was not cultured. Presumably the longer these foci have been present the longer they take to resolve. This may explain why relapses occurred in cases of relatively long duration before streptomycin treatment was started.

It therefore appears that it is justifiable to discontinue streptomycin when the C.S.F. has been sterile for at least a week in early moderately severe cases. Treatment may have to be prolonged, however, if the temperature is persistently raised, if there has been a long illness before the infection is controlled, if there is an active focus of infection, or if the response to treatment is slow. Unduly long courses of streptomycin may be avoided by combining it with sulphonamides. Both drugs could be used in the acute stage, after which a further course of sulphonamides may prove adequate in preventing a relapse.

Streptomycin Resistance

Alexander (1947) has shown that the development of a resistant strain of *H. influenzæ* is due to the elimination of all sensitive organisms and to the survival of the very few insensitive forms that occur in every large bacterial population. A few resistant organisms can be grown from nearly every case, but it is only in very severe infections that they succeed in establishing themselves. If this happens it usually follows shortly after the start of streptomycin therapy. Case 9 is an example of this type, the organism becoming resistant in forty-eight hours. There is no reason to suppose the dosage was inadequate, but it was remarkable that the C.S.F.-streptomycin levels remained persistently low despite big intrathecal doses. No resistant strains developed from any of the cases that relapsed. A sensitive strain was grown from case 7 after nineteen days' streptomycin therapy.

Combined therapy therefore seems to be indicated in severe infections, because a single chemotherapeutic agent may destroy a large proportion of the organisms but leave sufficient numbers to maintain the infection. The second drug, less effective by itself, may play a decisive part by destroying these remaining organisms. This is of paramount importance in severe *H. influenzæ* infection, since there are no indications of when a resistant strain may emerge. Theoretically, combined therapy with streptomycin, rabbit antiserum, and sulphonamides should prove most effective if given at the onset, when the number of streptomycin-resistant organisms is still small. If rabbit antiserum is not obtainable, a combination of streptomycin, penicillin, and sulphonamides may prove to be the treatment of choice.

SUMMARY

Streptomycin was given in 12 cases of *H. influenzæ* meningitis. One case is excluded because there was no bacteriological evidence of active infection on admission. Of the remaining 11 patients 3 died, and in 1 of these the organism became resistant to streptomycin.

The clinical picture is described with a view to earlier diagnosis and the recognition of severe cases.

Streptomycin gave good results in the mild or moderately severe cases but was unsatisfactory in 3 severe cases.

In 3 cases a relapse followed a full course of streptomycin. Factors that might predispose to a relapse are discussed, with particular reference to the duration of treatment.

In view of the failure of streptomycin in severe cases and of the possible development of resistant strains, it is recommended that all cases should be treated with streptomycin and sulphonamides. If there is any reason to suspect a severe infection, either antiserum or penicillin should be given in addition.

I wish to thank Dr. K. H. Tallerman, M.C., and Dr. R. H. Dobbs for permission to publish these cases; Prof. Clifford Wilson and Dr. F. C. O. Valentine for their valuable advice and guidance, and the latter also for the bacteriological investigations; and Dr. H. G. Dunn for his help and criticism.

REFERENCES

Alexander, H. E. (1943) *Amer. J. Dis. Child.* **66**, 172.
— (1944) *J. Pediat.* **26**, 517.
— (1947) *J. exp. Med.* **85**, 329.
— Leidy, G., Rake, G., Donovick, R. (1946) *J. Amer. med. Ass.* **132**, 434.
Beck, K. H., Janney, F. R. (1947) *Amer. J. Dis. Child.* **73**, 317.
Duncan, D. H., Webb, C. H. (1934) *J. Pediat.* **4**, 216.
Field, C. E., Rogers, H. (1936) *Bristol med.-chir. J.* **53**, 151.
Huntington, R. W. jun., Weiss, D. W. (1936) *J. Pediat.* **9**, 456.
Lindsay, J. W., Rice, E. C., Selinger, M. A. (1940) *Ibid*, **17**, 220.
Mutch, N. (1941) *Lancet*, ii, 751.
National Research Council (1946) *J. Amer. med. Ass.* **132**, 4.
Smith, M. H. D., Wilson, P. E., Hodes, H. L. (1946) *Ibid*, **130**, 331.
Turner, E. K. (1945) *Med. J. Aust.* i, 219.
Weinstein, L. (1946) *New Engl. med. J.* **235**, 101.
Williams, P., Tallerman, K. H. (1937) *Arch. Dis. Childh.* **12**, 263.
Zinnemann, K. (1946) *Brit. med. J.* ii, 931.

AN ARTIFICIAL HEART OR CARDIOPULMONARY MACHINE

PERFORMANCE IN ANIMALS

VIKING OLOV BJÖRK
M.D.

From the Surgical Clinic of Sabbatsberg Hospital, Stockholm, Sweden

IN experimental and clinical work which he began in 1935 Crafoord found it possible to suspend the flow of blood to all organs but the brain for a considerable time without damaging them. Thus, in 33 patients undergoing operation for patent ductus arteriosus he double-clamped the aorta for 10–27 min.—in most cases more than 20 min.—just below the point where the left subclavian artery arises, without causing any subsequent disturbances in the patients' internal organs.

In view of this experience Crafoord thought it possible to achieve a bloodless approach to the inside of the heart, arresting the circulation of blood but maintaining an adequate flow through the brain with a cardiopulmonary machine. In 1946 Crafoord and Andersson constructed an artificial heart, which I have studied in experiments on animals.[1] Thus in a dog I have clamped both superior and inferior venæ cavæ for 33 min., rendering the heart bloodless but maintaining the blood-flow to the brain alone with the cardiopulmonary machine. The dog survived with no sign of organic damage and became father to eleven puppies.

Though all the other organs will tolerate an arrest of the circulation for half an hour, a few minutes' anoxia damages the brain. During a bloodless intracardiac

1. Björk, V. O. (1948) *Acta chir. scand.* suppl. 137.

Digitized by Google

operation it is therefore necessary to maintain an adequate circulation of oxygenated blood through the brain with a perfusion apparatus capable of performing the work of both the heart and the lungs. In this cardiopulmonary machine the saturation with oxygen of a rapidly moving blood-stream must be achieved with the lowest possible destruction of red cells. At the same time physicochemical changes in the blood must be kept within normal limits.

THE APPARATUS

The main principle of the artificial blood-oxygenator is the brief exposure to oxygen of films of blood of as large an area as possible—i.e., the total area of blood film exposed per minute must be very large. In the apparatus we devised the blood flows through a trough occupying the lower part of a horizontal cylinder. This trough is divided into sections by partitions so made that the blood, passing from one section to the next, flows alternately over and under successive partitions (fig. 1). Through the cylinder runs a central axle bearing 40-50 discs in groups of 4 which dip into the blood and, as they rotate, expose new films of blood to the oxygen in the cylinder. This arrangement facilitates the mixing of oxygenated and unoxygenated blood. It also prevents some of the blood from remaining at the bottom of the trough throughout its passage through the cylinder. The upper part of the cylinder consists of a detachable tight-fitting lid of 'Plexiglass,' which allows the blood to be inspected at any time. The discs are of rhodium-plated stainless steel, 0·5 mm. thick, 13 cm. in diameter, and 4 mm. apart (closer discs were found to cause foaming). The axle is rotated at about 120 r.p.m. by a 40-watt electric motor.

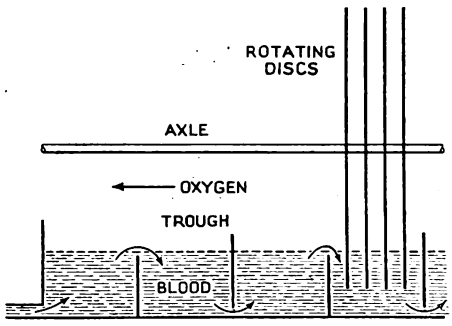


Fig. 1—Scheme of circulation through the oxygenating cylinder.

The pump (fig. 2) consists of a metal cylinder with a rubber cuff on the inside. The rubber tube for the blood passes through the centre of this cuff between two valves, made of a thin rubber band on a metal frame. The pumping action is attained by rhythmically inflating the cuff with compressed air, so squeezing the rubber tube.

The perfusion apparatus is shown in fig. 3, in which tube 1 conveys venous blood from the animal to a 20 ml. glass cylinder (2) and the rate of blood-flow can be determined by measuring the time taken by the blood to fill the cylinder when the tube to the oxygenator is closed and an air outlet is opened. From this cylinder the blood enters the oxygenator (3). Oxygen is supplied through a flow-meter; it is warmed in a metal tube passing over two 150-watt bulbs and travels in the opposite direction to the blood. There are two outlets for blood from the oxygenator. One (4) leads into a glass tube in front of a photo-electric cell, which keeps the blood in the oxygenator at about the same level by regulating the speed of the pumps. This blood re-enters the main blood-stream at 5, so that there is a continuous circulation of blood in these side tubes; otherwise the sedimentation of red cells would produce a translucent layer of plasma at the top of the blood in front of the photo-electric cell, which would then act incorrectly.

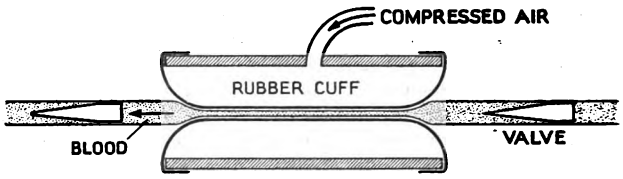


Fig. 2—Diagram of pump.

The saturated blood leaves the oxygenator through tube 6, which divides into two parallel tubes, passing through the pumps (7), which work in parallel with alternate pulsations. The two blood-streams next combine and pass through a filter. Subsequently the blood passes between the walls of a double-walled glass cup (8) containing the contact thermometer, the remaining space in the cup being filled with oil. There is a branch leading to a manometer (9) for blood-pressure reading. Before entering the artery through tube 10, the blood passes through a glass vessel, where any small air-bubbles are removed.

Latex surgical rubber tubing, with glass connexions, is used. All glassware, rubber tubing, valves, and the trough are coated with silicon to give them a smooth and water-repellent surface. A solution of $(CH_3)_2Si(OH)_2$ and $CH_3Si(OH)_3$ in the proportion of 9 : 1 ('Siloxan UHB 300,' Swedish patent 3408/48) is used.

RESULTS

The rate of gas-flow through the oxygenator was found to have no significant effect on oxygenation or on the elimination of carbon dioxide. Experiments with various mixtures of oxygen, nitrogen, and carbon dioxide showed that an increase in the partial pressure of oxygen in the oxygenator improved oxygenation but had no effect on the elimination of carbon dioxide, which depended on the partial pressure of carbon dioxide in the gas used. Raising the temperature improved both oxygenation and the elimination of carbon dioxide. The optimal duration of exposure of each blood film to oxygen in the oxygenator was found to be 0·4–0·5 sec. An increase in the number of rotating discs increased the oxygenation.

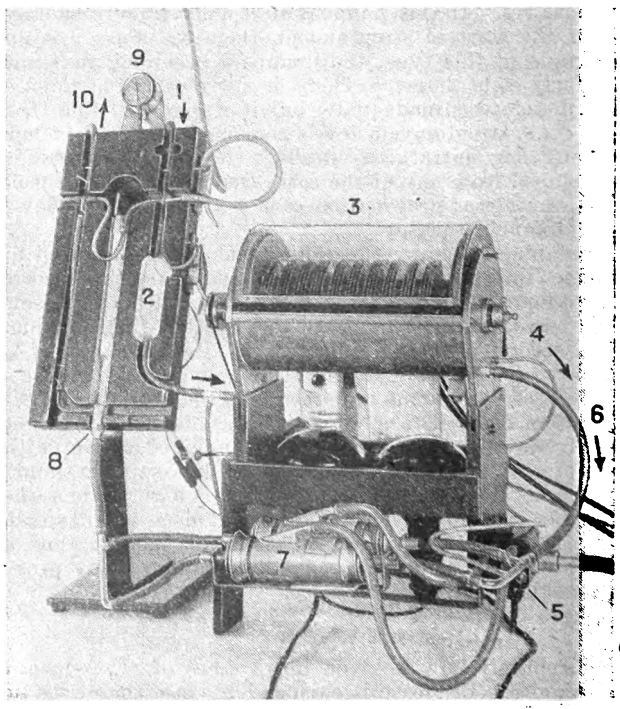


Fig. 3—The cardiopulmonary machine.

Digitized by Google

Loss of water in the oxygenator was compensated by adding fluid to the blood with a drip feed during the perfusion. The disadvantages of hæmolysis, which sometimes persisted despite every precaution, were diminished by using pure oxygen in the oxygenator, sodium bicarbonate solution being added to the blood by a drip feed to make the animal's urine alkaline. The unavoidable hæmolysis in the perfusion apparatus was well within the limits of what can be tolerated in brain-perfusion experiments. There was also some destruction of leucocytes, the lymphocytes being more resistant to mechanical trauma than the granulocytes. The thrombocytes were not significantly affected.

There was a considerable fall in blood-sugar during the circulation of blood in the perfusion apparatus. Since the anoxic brain is especially sensitive to hypoglycæmia, glucose solution was added by means of a drip feed.

In the experiments on animals the perfusion apparatus was first filled with blood taken from donor dogs and filtered through a 'Monell' filter (mesh 150 × 150 μ). The blood in the apparatus was mixed with the dog's own blood and filtered through the dog's own lungs before brain perfusion was begun. The technique was as follows. The blood from the apparatus was pumped through the right external jugular vein into the superior vena cava and after traversing the lungs was withdrawn from one of the common carotid arteries. Thus, when brain perfusion started the perfusion apparatus contained the dog's own blood, mixed with donor blood which had been filtered through the perfused dog's lungs. During the perfusion continuous filtration through a filter of mesh 300 × 300 μ was used, as a guarantee against embolism.

The apparatus has been tested in animals and found capable of completely maintaining the circulation through the brain for a sufficient time to permit bloodless intracardiac operations. In three dogs the vertebral arteries and veins on both sides were divided at the first stage of a two-stage operation. After about 10 days the brain was perfused through the left common carotid artery, the right being clamped for 25, 63, and 93 min. The venous cannula was inserted into the superior vena cava through the right external jugular vein. After the brain had been perfused, nothing abnormal could be detected during 5–7 months' observation.

With both the superior and the inferior venæ cavæ occluded and the azygos vein ligated, the brain was perfused for 33 min. with no ill effects on the dog. Seven dogs have survived perfusion of the brain with the cardiopulmonary machine.

SUMMARY

Animal experiments have proved that the perfusion apparatus described can perform the functions of heart and lungs for a sufficient time to permit bloodless intracardiac operations. Dogs have shown no ill effects after halt an hours' perfusion of the brain.

"... One finds most of the defenders of 'family integrity' in the wealthier groups of society at the moment and it is not difficult to discern that, in many instances, the members of those wealthier groups do, at their own expense, precisely what they condemn in the other groups for whom the community makes the corresponding provision. If it is right to employ a 'nanny,' it is right to send a child to a nursery. If it is right to dine at the Savoy, it is right to dine at a British Restaurant. If it is right to call in Sir X. Y. from Harley Street to look at a child who ails little or nothing, it is right to take a child to a welfare clinic. All that remains of the argument against State or community help for the family is that nobody should receive what he cannot pay for out of his own pocket. In other words, the objection is to 'pauperisation' as it used to be called, which is a matter very different from the 'disintegration of the family.'"—*Medical Press*, Sept. 15, 1948, p. 193.

ABSORPTION AND EXCRETION STUDIES WITH RADIOACTIVE PENICILLIN

S. ROWLANDS, Ph.D., B.Sc. Lpool
PHYSICS DEPARTMENT.

D. ROWLEY, Ph.D., B.Sc. Lond.
WRIGHT-FLEMING INSTITUTE

H. C. STEWART, M.A., M.D. Camb., Ph.D. Lond.
PHYSIOLOGY DEPARTMENT

St. Mary's Hospital Medical School, London

WHEN penicillin is given parenterally it is rapidly excreted and a variable amount, up to 70%, is found unchanged in the urine (Topley and Wilson 1945). It is not known what happens to the remainder, and the weight of material involved is so small as to make this problem practically insoluble by ordinary chemical methods. Recently, penicillin containing the radioactive sulphur isotope, S^{35}, has been prepared (Rowley et al. 1948), and with this material the fate of the penicillin molecule can be followed by methods independent of biological activity.

The first experiments were designed to determine the excretion path of penicillin after intramuscular injection; then, with this information, to probe the more difficult problem of excretion of penicillin given by mouth.

For our experiments female cats were chosen, since they can easily be catheterised and produce a workable volume of urine. Premedication was given in the form of intraperitoneal urethane, 0·5 g. per kg. of body-weight, which sufficed to keep the cats docile. Immediately after the injection of penicillin the bladder was emptied with a glass catheter, the sample being discarded. Thereafter the cats were catheterised at intervals of 1 or 2 hours for 8–10 hours, the whole procedure being carried out as aseptically as possible.

Assay of Radioactivity

The radioactive penicillin used was labelled with sufficient S^{35} to enable the accurate detection of about $^1/_{30}$ unit with a Geiger counter (1 unit of penicillin was equivalent to 1100 disintegrations per min.).

The radioactivity of the samples was measured with a Geiger-Muller counter and scale-of-a-hundred recording circuit.

TABLE I—URINARY EXCRETION OF INTRAMUSCULAR PENICILLIN

Cat no.	Time	Volume of urine (ml.)	Total activity in sample (units)		Remarks
			Geiger-pen	Bio-pen	
2	2 hr. 0 min.	19	330	180	Penicillin 650 units injected. Samples were not corrected for self-absorption of β rays in this expt. *Recovery*: Geiger-pen, 72%; Bio-pen, 47%
	3 hr. 30 min.	6	96	84	
	5 hr. 0 min.	14	22	29	
	6 hr. 10 min.	6	9	10	
	8 hr. 0 min.	11	13	8	
	Total	*recovery*	470	311	
3	1 hr. 40 min.	4·5	121	72	Penicillin 700 units injected. *Recovery*: Geiger-pen, 101%; Bio-pen, 60%
	3 hr. 5 min.	14·0	515	308	
	5 hr. 5 min.	36·0	67	35	
	6 hr. 50 min.	21·0	6	10	
	Total	*recovery*	709	425	
4	1 hr. 50 min.	5·0	540	350	Penicillin 680 units injected. *Recovery*: Geiger-pen, 100%; Bio-pen, 66%
	3 hr. 45 min.	3·5	112	90	
	5 hr. 45 min.	4·0	27	8	
	Total	*recovery*	679	448	
5	1 hr. 40 min.	3·0	279	120	Penicillin 680 units injected. *Recovery*: Geiger-pen, 98%; Bio-pen, 36%
	3 hr. 20 min.	4·0	212	80	
	5 hr. 15 min.	14·0	134	28	
	6 hr. 40 min.	7·5	24	7·5	
	8 hr. 0 min.	16·0	19	0	
	Total	*recovery*	668	235·5	

Digitized by Google

S^{35}, an isotope with a half-life of 87 days, emits β rays of small penetrating power. In measuring such soft radiations difficulties are encountered owing to the absorption of the β rays both in the window of the Geiger counter and in the material of the sample (self-absorption). The former difficulty was largely overcome by using on the counter a very thin mica window through which the radiations could pass readily. To correct for self-absorption samples containing known amounts of S^{35} mixed with known amounts of absorbing material were assayed. From these results a graph was drawn relating loss from self-absorption to weight of the sample. In this way correction could be made for self-absorption in each of the samples measured. To ensure the greatest possible accuracy the procedure was designed to keep this correction as small as possible. In preparing for radioactive assay each sample was diluted to $^1/_6$ with distilled water, and 100 c.mm. was pipetted on to a nickel planchette and dried by heating at 130°C for 15 min. The planchettes were kept in a desiccator over calcium chloride until the actual counting, since they were found to absorb water vapour, so increasing the self-absorption of the material.

To minimise statistical errors, at least 5000 counts were taken with each sample, and each count was continued for more than 5 min., to give a timing error less than the statistical error. The total error in the radioactive assay of each sample was less than 5%.

Biological Assay

For our purposes the plate method (Fleming 1942) was satisfactory. As Heatley (1944) has shown, there may be an error in this method of ± 30%. Estimation was greatly facilitated in our case by our knowing from previous radioactive measurements the approximate concentration of penicillin to be expected. The amount of penicillin in the pooled samples from each cat was doubly checked by extraction with an equal volume of amyl acetate at pH 2·5 to remove 95% of the biological penicillin (Rowley et al. 1946). The number of units extracted corresponded exactly to the sum of the individual bio-assays. Through this double check the error in our bio-assays is likely to be less than the figure given above.

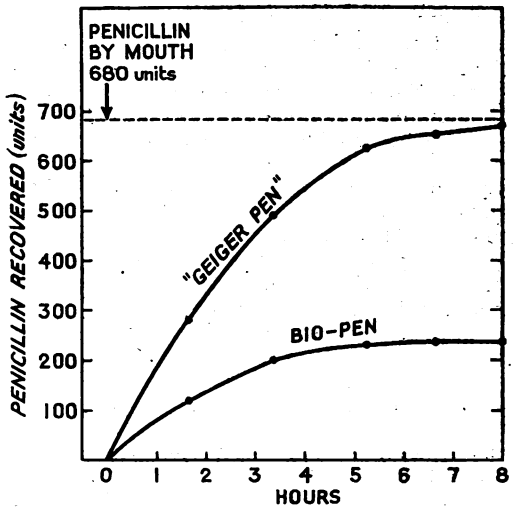
TABLE II—URINARY EXCRETION OF PENICILLIN GIVEN BY MOUTH

Cat no.	Time	Volume of urine (ml.)	Total activity in sample (units)		Remarks
			Geiger-pen	Bio-pen	
6	1 hr. 35 min.	5·5	60	40	Penicillin 650 units given by mouth in 5 ml. of total fluid. *Recovery:* Geiger-pen, 54% Bio-pen, 25%
	3 hr. 10 min.	21·5	118	97	
	4 hr. 35 min.	40·0	132	20	
	6 hr. 5 min.	20·0	26	0	
	8 hr. 0 min.	15·0	12	0	
	Total recovery		348	157	
7	1 hr. 35 min.	25·0	235	50	Penicillin 2600 units given by mouth in 20 ml. of total fluid. *Recovery:* Geiger-pen, 24% Bio-pen, 10%
	3 hr. 25 min.	3·5	224	140	
	5 hr. 15 min.	3·5	115	49	
	6 hr. 30 min.	2·0	27	8	
	8 hr. 0 min.	4·0	36	4	
	Total recovery		637	251	
8*	2 hr. 20 min.	1·9	105	114	Penicillin 650 units given by mouth in 5 ml. of total fluid. *Recovery:* Geiger-pen, 36% Bio-pen, 36%
	4 hr. 0 min.	2·7	81	81	
	5 hr. 45 min.	4·0	44	40	
	7 hr. 0 min.	1·0	7	2	
	Total recovery		237	237	
9	2 hr. 10 min.	3	46	18	Penicillin 560 units given by mouth in 5 ml. of total fluid. *Recovery:* Geiger-pen, 37% Bio-pen, 7%
	4 hr. 5 min.	15	73	22	
	5 hr. 30 min.	16	60	0	
	7 hr. 0 min.	29	30	0	
	Total recovery		209	40	
0	1 hr. 25 min.	17·0	7	...	Penicillin 590 units given by mouth in 8 ml. of total fluid. Recovery of Geiger-pen: urine 24%, gut† 59%
	3 hr. 5 min.	1·5	30	...	
	4 hr. 40 min.	1·8	52	...	
	6 hr. 10 min.	2·2	52	...	
	Total recovery		141	...	

* Repeat of cat no. 7.

† Cat no. 10 was killed, and Geiger-pen units were determined in the contents of its whole gastro-intestinal tract, as follows:

		Geiger-pen (units)
Stomach	Vol. 60 ml.	166
Small gut	Vol. 80 ml.	183
Large gut	Vol. 80 ml.	0
		349



Urinary excretion of penicillin given by mouth to cat 5.

EXPERIMENTAL RESULTS

For easy comparison the radioactivity in the various urines has been back calculated into "Geiger-penicillin units" on the basis of 1100 disintegrations per min. being equivalent to 1 unit of penicillin. Some of this radioactivity was present as penicillin breakdown products; the amount of this non-penicillin radioactivity was calculated by subtracting the biological-penicillin (bio-pen) level from the "Geiger-penicillin" (Geiger-pen) level.

Intramuscular Injection.—The results of intramuscular injections of labelled penicillin are summarised in table I; the excretion curve from cat 5 is shown in the accompanying figure. It is apparent from these results that the difference between the amount of penicillin injected and that which appears as bio-pen in the urine is represented by breakdown products of penicillin excreted in the urine as rapidly as the penicillin itself.

Penicillin by Mouth.—In these experiments, solid food having been withheld for the previous 24 hours, the penicillin was given by stomach-tube and washed down with an equal volume of water. Otherwise the technique was the same as before.

The results of these experiments, summarised in table II, show that, when penicillin is given by mouth, by no means all the penicillin or its breakdown products are recovered from the urine. In cat 10 an attempt was made to determine whether this was due to retention in the intestinal lumen. Six hours after penicillin had been given by mouth the cat was killed and the radioactivity of the contents of various portions of the gut determined after thoroughly washing through the gut with water. It was found that 59% of the original radioactivity still remained in the gut, whereas 24% had appeared in the urine. In spite of the fact that urinary excretion had not finished, the presence of such a large proportion of the original activity in the gut after six hours strongly suggests that non-absorption from the gut is the reason for the low urinary excretions after penicillin has been given by mouth.

DISCUSSION

The experiments with intramuscular penicillin clearly show that it is not stored in the body at all but is quickly excreted, partly as penicillin and partly as penicillin

Digitized by Google

breakdown products. Stewart and May (1947) concluded that "The most important factor influencing the absorption of penicillin [given by mouth] seems to be the unexplained individual variations in the absorptive capacity of the gut." From the present work it seems that once the penicillin has crossed the intestinal wall it behaves in a manner exactly similar to injected penicillin. It has been shown that the scanty excretion of penicillin given by mouth can largely be explained by incomplete absorption. Further studies directed towards improving absorption from the gut therefore seem to be worth while.

SUMMARY

Urinary excretion studies were carried out in female cats using penicillin labelled with S^{35}.

Intramuscular injections of ordinary and labelled penicillin gave rise to a urinary excretion of 100% of the radioactive sulphur isotope, but to a much smaller recovery of penicillin.

There was no evidence of retention of penicillin in the body as the radioactive breakdown products were excreted over the same time interval as the penicillin.

When the labelled penicillin was given by mouth much less was excreted; the amount of radioactivity remaining in the gut at the end of the experiment suggested that non-absorption would account for the penicillin not found in the urine.

We wish to thank Sir Alexander Fleming for his continued interest in the work; the Medical Research Council for the generous gift of S^{35}; E. Lester Smith, D.SC., for the preparation of the radioactive penicillin; Messrs. P. Roberts, B.SC., and P. D. Cooper, B.SC., for valuable assistance; and the Drummond Research Fund (D.R.) and the Sir Halley Stewart Trust (H.C.S.) for their continued financial support.

REFERENCES

Fleming, A. (1942) *Lancet*, i, 732.
Heatley, N. G. (1944) *Biochem. J.* 38, 61.
Rowley, D., Miller, J., Rowlands, S., Lester-Smith, E. (1948) *Nature, Lond.* 161, 1009.
— Steiner, H., Zimkin, E. (1946) *J. Soc. chem. Ind., Lond.* 65, 237.
Stewart, H. C., May, J. R. (1947) *Lancet*, ii, 857.
Topley, W. W. C., Wilson, G. S. (1945) Topley and Wilson's Principles of Bacteriology and Immunity. 3rd ed., London; p. 184.

INTESTINAL OBSTRUCTION DUE TO ASCARIASIS

REPORT OF A CASE

KHALID NAJI
B.M., M.S.
RESIDENT SURGICAL OFFICER, TEACHING HOSPITAL, BAGDAD

A BOY, aged 14, a labourer, was admitted to this hospital with thirty-six hours' history of abdominal colic, which had increased in intensity for twenty-four hours, with vomiting on six occasions and no passage of flatus or fæces in the last twenty-four hours. His last motion had been mixed with blood. For two months he had been losing weight and strength. He had previously passed long worms in his stools and had had attacks of colic during the last two months. After treatment by his doctor he had passed about 15 roundworms. Other members of his family had also passed roundworms. The patient had no history of any other disease.

On admission the patient was anæmic, looked ill, had attacks of colic every few minutes, and vomited a roundworm. No cyanosis, no jaundice, no dyspnœa, no œdema, no clubbing of fingers. Temperature over 101°F, pulse-rate 120 per min., respirations 26 per min., blood-pressure 120/80 mm. Hg. Tongue furred and moist; teeth and tonsils clean and normal. Abdomen moved freely on respiration; slight bulge in right hypochondrium and epigastrium; peristalsis visible during colic, when a sausage-shaped mass was also seen in the epigastric and both hypochondriac areas. This mass was tender on palpation and dull on percussion, rest of abdomen being soft, not tender, and resonant on percussion. Spleen not palpable; liver not enlarged. Peristaltic sounds heard on auscultation. Nothing abnormal detected per rectum except bloodstained mucus. Heart and lungs normal.

Treatment.—Two enemas produced neither flatus nor fæces. The patient was given morphine gr. $^1/_6$ and atropine gr. $^1/_{200}$ and prepared for laparotomy, intussusception having been diagnosed.

Operation.—Under general anæsthesia, induced with chloroform and continued with ether, a right paramediar incision was made, extending $2^1/_2$ in. above and below level of umbilicus. When peritoneum was incised, 2 ft. of much distended small intestine bulged out. Intestinal wall of the loop was so thin that it was transparent, revealing a compact mass of roundworms. Loop was 2 ft. proximal to ileocæcal junction; associated mesenteric lymph-glands enormously enlarged. Owing to thinness of intestinal wall and danger of rupture on manipulation I packed the peritoneal cavity; I then made a 2 in. incision in middle of loop, and evacuated 402 roundworms with sponge forceps. Loop was repaired with double layer of continuous sutures, and abdomen was closed. Operation lasted 55 min.

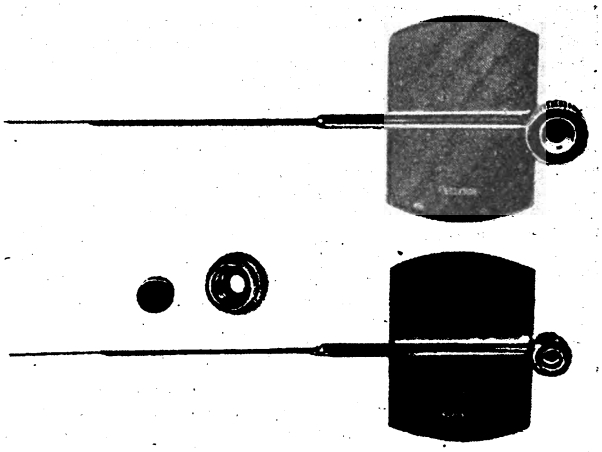
Postoperative Treatment.—To prevent ileus, the patient was given continuous rectal saline, and morphine gr. $^1/_6$ at midnight. Next day he was started on pituitary extract 0·5 ml. twice daily, and had acetylcholine 1 ml. twice. On third day rectal saline was stopped and fluid was given by mouth. On fourth day a morning enema produced fæces; temperature normal; pulse-rate 90. On fifth day pituitary extract was stopped, and the patient was given light diet and a morning enema. On seventh day the patient was given santonin gr. 6 followed by castor oil, and four roundworms were passed. Santonin gr. 3 and castor oil was given on eighth and ninth days, and on ninth day 19 roundworms were passed. Full diet was given, and stitches were removed, on tenth day. The patient was discharged from hospital on fourteenth day.

New Inventions

CANNULA FOR REPEATED INTRAVENOUS INJECTIONS

REPEATED intravenous injections always entail discomfort to the patient, especially if they are made many times at the same site, when hæmatoma is often unavoidable. To the physician who performs the injections the insertion of the needle into the vein sometimes offers serious difficulties. To render the procedure more acceptable to the patient and easier for the physician, the cannula illustrated here has been devised.

The instrument consists of a narrow-gauge cannula let flush into a metal plaque. The blunt end of the cannula is bent through 90° and bears a circular flange over which a rubber diaphragm 1 mm. thick can be fixed with a screw cap. The point of the cannula having been inserted into the vein, the injections are carried out with an ordinary needle easily, and without inconvenience to the patient, through this rubber diaphragm.



Digitized by Google

It is advisable to remove the cap and diaphragm before inserting the point of the cannula into the vein so that escaping blood will show that the point of the cannula has entered the lumen of the vein. The cannula is kept in place with strips of tape crossing the metal plaque. The rubber diaphragm can easily be changed for a fresh one after a considerable number of injections. The cannula can be inserted at any site, but preferably into the dorsum of the hand or the forearm, and can be left there for several days.

Hitherto its most extensive use has been in heparin treatment and general intravenous anæsthesia. It has also been adopted for protracted intravenous infusion and blood-transfusion. For several years this cannula has been used extensively in the surgical departments of the Swedish hospitals. At Serafimerlasarettet in Stockholm it is used in practically all operations. All intravenous injections during operation are given with it. When it is used for infusions during operation, the person giving the infusion should steady with his hand the infusion needle through which the liquid is introduced into the cannula. After each injection the rubber diaphragm is cleaned with alcohol or ether; the cannula may also be protected with sterile surgical gauze. The cannula is used daily in our operation services and, so far as I know, there has never been a case in which septicæmia could be attributed to it.

Stockholm. THORE G. OLOVSON, M.D.

Reviews of Books

Lecture Notes on Pharmacology

J. H. BURN, M.D., F.R.S., professor of pharmacology, University of Oxford. Oxford: Blackwell Scientific Publications. 1948. Pp. 128. 6s.

IT may be doubted whether many students, grappling with standard works on pharmacology, share Elia's affection for big books. "And you my midnight darlings, my Folios! must I part with the intense delight of having you (huge armfuls) in my embrace?" In his preface Professor Burn rightly deplores the fact that "almost all medical textbooks are longer than they should be." He might have added that too few teachers seem to appreciate the student's difficulty when confronted with the task of reading a completely new subject. This is a readable little book, and despite its brevity it has the merit of being comprehensive and up to date. It should prove invaluable as a companion to standard textbooks on the subject; but the student who thinks that these lecture notes provide a convenient substitute for the "huge armfuls" is courting disaster by underestimating the perspicacity of his examiners.

Hutchison's Food and the Principles of Dietetics

(10th ed.) V. H. MOTTRAM, M.A., formerly professor of physiology, King's College of Household and Social Science, University of London; GEORGE GRAHAM, M.D., F.R.C.P., consulting physician, St. Bartholomew's Hospital. London: E. Arnold. 1948. Pp. 727. 21s.

TEN years ago, general nutrition occupied about a seventh of this book; today—reflecting many important advances—it occupies more than a third. New chapters on the hygiene and processing of food insist refreshingly on the variability of the individual and the uncertainty of much of our knowledge. Professor Mottram might have explained earlier, though, that the figures given by the National Research Council of the U.S.A. are not requirements but recommended allowances—"a tentative goal towards which to aim." Much of the dogma which mars books on nutrition is absent here, but a little remains. It is not at all certain, for example, that vitamin C really is concerned in the oxidation-reduction systems of the body; indeed, several items in this first section of the book are out of date.

The section describing the properties of food distinguishes this book from almost all others concerned with dietetics, and is extremely useful. One or two other sections are less satisfactory, but also as a whole this classical work still keeps its place among the best and most informative books on the subject.

The Aseptic Treatment of Wounds

C. W. WALTER, M.D., assistant professor of surgery, Harvard University. New York and London: Macmillan. 1948. Pp. 372. 45s.

As the late Elliott Cutler says in his foreword, this book contains "information of the utmost value to everyone who is concerned with the surgical care of patients, whether it be the surgeon, the nurse, the medical student, or the hospital superintendent." It describes the principles of aseptic surgery and the methods of putting those principles into practice. Surgeons are apt to accept the sterilised dressings, powders, gloves, and other materials handed to them as unquestionably sterile without inquiring into the methods used for making them so. The intricacies of this apparently simple procedure are soon realised by anyone responsible for setting up arrangements for carrying out aseptic surgery. This book goes into the technique of sterilisation in all its aspects and also into the details of procedure in both the operating-theatre and the wards. Moreover every step of the nurse or surgeon is depicted in clear line drawings. The teaching in this book will provide a sound basis for the instruction of nurses, students, surgical dressers, or others who are to take part in modern operations.

Textbook of Anæsthetics (7th ed. Edinburgh: E. & S. Livingstone. 1948. Pp. 568. 30s.).—This book by Dr. R. J. Minnitt and Dr. John Gillies has become one of the standard textbooks in the English language. In addition to a general revision of the text, the section on local and regional analgesia has been enlarged, and a useful chapter on curare has been added.

Recent Advances in Cardiology (4th ed. London: J. & A. Churchill. 1948. Pp. 454. 24s.).—Dr. Terence East and Dr. Curtis Bain have entirely rewritten this new edition, which is naturally longer than its predecessor of 12 years ago. The authors' own views are interwoven with, though kept largely subsidiary to, a large number of references to recent work; no important modern paper remains unquoted, however briefly. The chapter on congenital heart disease deals relatively fully with a topical subject in which knowledge and treatment are now advancing hand in hand; and a final chapter on the latest methods of cardiography discusses unipolar leads and vector cardiograms.

Cardiovascular Diseases (2nd ed. London: Heinemann Medical Books. 1948. Pp. 743. 63s.).—In its new edition this book is at least twice the length of the first, and it has now become a comprehensive textbook of cardiology. A considerable section on peripheral vascular disease has been added and also a large bibliography. Prof. David Scherf and Prof. Linn J. Boyd, of the New York Medical College, quote workers of all nationalities, yet have their own clear-cut views on all aspects of the subject; and it is this imprint of their personality which gives the book a welcome freshness. Its clear and thoughtful style (apart from one or two ambiguities which persist from the first edition), and the attempt to assign a physiological reason for symptoms whenever possible, give it a place in the front rank of cardiological textbooks.

Diseases Affecting the Vulva (3rd ed. London: H. Kimpton. 1948. Pp. 204. 25s.).—Written by a dermatologist of wide experience, this useful book provides for other dermatologists a systematic text on skin conditions of the vulva, and reminds the gynæcologist that vulvar lesions are identical with lesions elsewhere on the skin surface. Dr. Elizabeth Hunt points out that abnormalities of the vulvar skin may well be localised manifestations of a general reaction or due to local irritants—often used in the course of mistreatment. The gynæcological aspects are well presented and the coloured photographs reliable. Caruncle, however, is an exception, and there is no mention of the excellent results which follow extended lymphadenectomy for carcinoma of the vulva (Bassett's operation). Dr. Hunt believes that kraurosis vulvæ is only a late or modified stage of leukoplakia which is itself lichen sclerosis modified by site. With this in view, she deprecates the use of excessive œstrogen dosage in this and allied conditions, and advises against vulvectomy, except in the case of proven carcinoma. As before, many useful prescriptions are included in the text and a general review of therapeutic methods is given as an appendix.

Digitized by Google

TRADE MARK

'THEOGARDENAL'

BRAND

theobromine and phenobarbitone

tablets

The vaso-dilator action of theobromine and the sedative action of phenobarbitone are combined in an effective synergistic form in 'THEOGARDENAL'.

In therapeutic doses it is non-toxic, has no cumulative effect, and is well tolerated even when prescribed over lengthy periods.

tablets: *(theobromine gr. 5 and phenobarbitone gr. ½)*

Containers of 25, 100 and 500

manufactured by

MAY & BAKER LTD

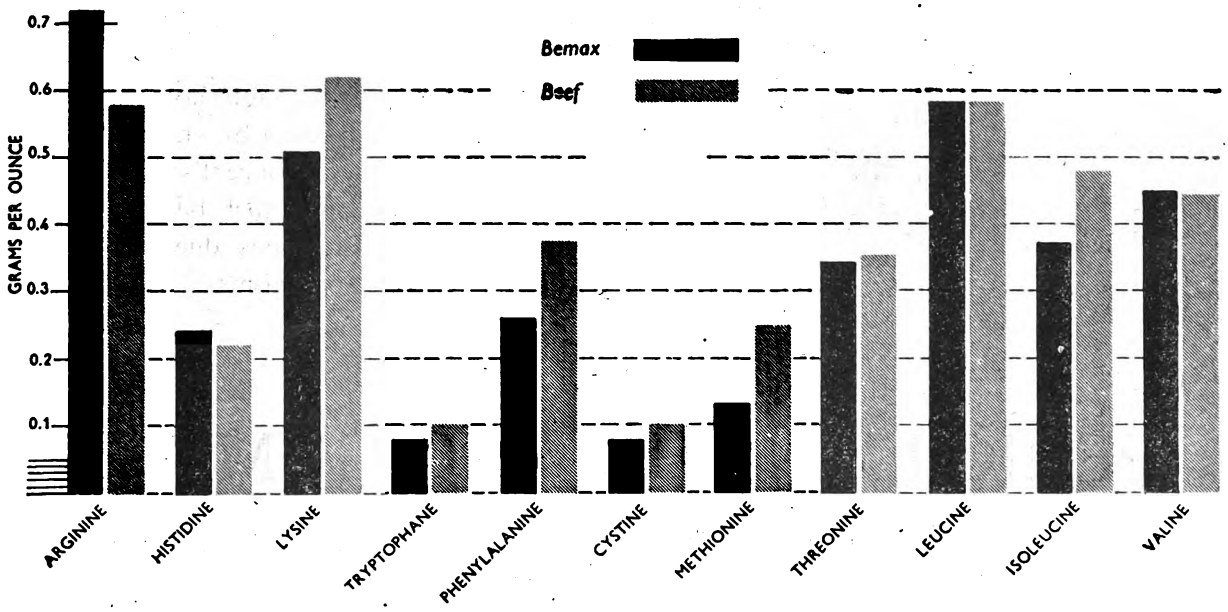
distributors

PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD. DAGENHAM

47286

What is a "first-class" protein?

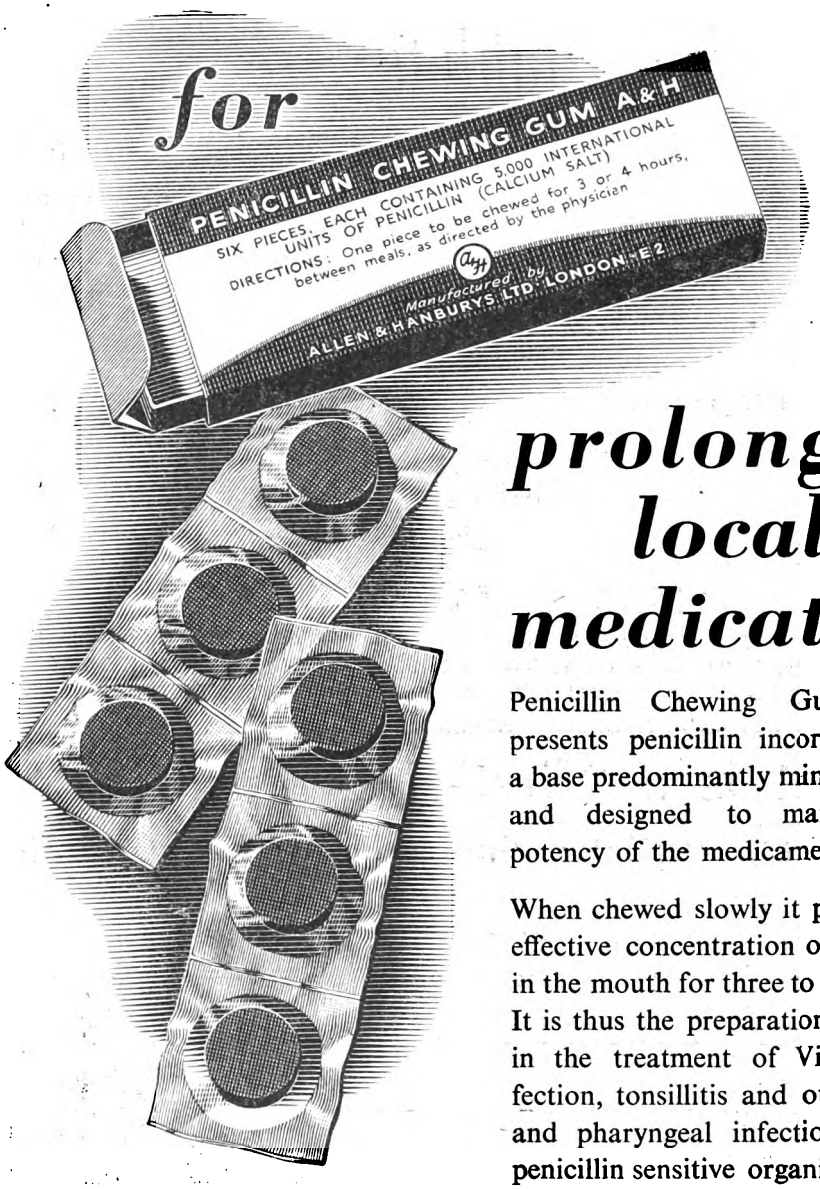
Compare the essential amino acids of beef and Bemax



Full documentation and/or clinical sample of Bemax may be obtained on application to Medical Dept. 48.B. Vitamins Limited, Upper Mall, London, W.6.

This announcement, the chart and the analyses are copyright.

Digitized by Google



prolonged local medication

Penicillin Chewing Gum A & H presents penicillin incorporated in a base predominantly mint-flavoured and designed to maintain the potency of the medicament.

When chewed slowly it provides an effective concentration of penicillin in the mouth for three to four hours. It is thus the preparation of choice in the treatment of Vincent's infection, tonsillitis and other buccal and pharyngeal infections due to penicillin sensitive organisms.

PENICILLIN CHEWING GUM A & H

In packets of six pieces, each piece containing 5,000 i.u. penicillin (calcium salt).

ALLEN & HANBURYS LTD · LONDON · E·2
TELEPHONE: BISHOPSGATE 3201 (12 LINES). TELEGRAMS: GREENBURYS, BETH, LONDON

Digitized by Google

THE LANCET

LONDON: SATURDAY, SEPT. 25, 1948

Penicillin in Syphilis

FIVE years have passed since penicillin was first used in syphilis, and it is doubtful whether its value can be fully assessed for at least another five. Yet, in spite of some early doubts and disappointments, it has been accepted almost universally and there can be no doubt that it has come to stay. In the United States a report,[1] based on the treatment of half a million cases, assesses the present position. Crystalline penicillin II (G) is regarded as superior to the impure commercial product, and it is best given intramuscularly in doses of 20,000 to 100,000 units dissolved in sterile water or isotonic saline every two or three hours day and night. The alternative is to inject a suspension of calcium penicillin in arachis oil with 4·8% beeswax in a daily dose of 600,000 units. The first method requires admission to hospital and the dose recommended for early syphilis is 4·8 million units given in 96 doses, each of 50,000 units at two-hour intervals day and night for eight days. With oil-wax mixture the daily dose is given for ten days, the total dosage being 6 million units. With both methods, when penicillin is used alone, the failure-rate of resistant cases and relapses is about 15% at the end of a year. The addition to this treatment of arsphenoxide given intensively in the form of 8 injections each of 60 mg. daily or every other day, and bismuth subsalicylate in 5 doses each of 0·2 g. every two or three days, does little to diminish the failure-rate. With additional fever therapy results have been little better, but this supplementary treatment adds to the difficulty of getting patients to coöperate.[2] Such accessory methods also involve increased risks to the patient and are therefore reserved for resistant cases, in which they are combined with more penicillin.

For latent syphilis, in which the duration of infection is often uncertain, penicillin has been used in the same dosage on the assumption that it will heal undetected lesions and may prevent the development of clinical manifestations later. It seems to be no more effective than arsenicals and bismuth in converting positive serum tests to negative in cases of late and latent infection, a finding which accords with the experience of WILLCOX[3] in this country. Penicillin has proved as effective as older remedies in healing the cutaneous, mucous, osseous, and visceral lesions of so-called benign late syphilis; but with these conditions, as with latent syphilis, many years must pass before statistics can show whether it will secure a good ultimate prognosis. The same applies to cardiovascular syphilis, and the possibility of dangerous Herxheimer reactions remains where syphilitic aortitis is complicated by aortic regurgitation, saccular aneurysm, or involvement of the coronary ostia; in such cases penicillin, if it is used at all, should only follow protracted treatment with heavy metals. For neurosyphilis of the meningeal and vascular types a dosage of 4–10 million units is recommended, given in aqueous solution over a period of seven to twenty-one days without adjuvant treatment. For parenchymatous neurosyphilis 10–20 million units is given in twelve to twenty days, accompanied by malaria therapy unless this is contra-indicated. In neurosyphilis of all kinds intramuscular administration seems to be as effective as intrathecal and is certainly much safer. For the prevention of syphilis in the unborn child penicillin has been remarkably successful and seems to be almost fully effective at whatever stage of pregnancy it is given. Dosage varies from 4·8 to 6 million units, given in aqueous solution at intervals of two to three hours over eight to fifteen days. Additional treatment is regarded as unnecessary and undesirable. For infantile congenital syphilis penicillin in aqueous solution is given every two or three hours day and night in a total dosage of 100,000 to 400,000 units per kg. of body-weight over one to two weeks. The results are excellent and the death-rate has been no higher than with other methods, most deaths being attributable to nutritional difficulties or intercurrent disease. For the later manifestations of congenital syphilis the results with penicillin have been much the same as in late acquired syphilis, and the ultimate outcome in these cases remains equally in doubt. Like other forms of treatment penicillin is of uncertain value for interstitial keratitis.

Penicillin has the outstanding advantage that, as its toxic effects are few and not dangerous, a massive dosage can be given in a short time. Because of its safety and its prompt and satisfactory effect it may now be accepted as the remedy of choice for syphilitic pregnant women and for infants with congenital syphilis. In cases of benign tertiary syphilis the patient's immunity processes have already given him a large measure of protection, and treatment will readily restore a temporary loss of balance between infection and immunity. Here penicillin appears to have great advantages whether used alone or supplemented by other measures. The chief outstanding problem is whether we are justified in treating early syphilis with penicillin alone, for at this stage the immunity reactions are not fully developed and insufficient treatment may be worse than none. The verdict in the United States so far is in favour of penicillin alone, and it may be said that this treatment is free from danger, the proportion of successes seems reasonably high, and the short duration of treatment throws into sharp relief the small number of cases which are likely to be resistant to any form of treatment and will require special measures.

In most British clinics the practice is to supplement adequate penicillin therapy with at least one full course of arsenicals and bismuth, given in weekly doses for ten weeks or so. This prolongs treatment considerably and increases its dangers. If it can be shown that this procedure greatly reduces the incidence of failures then it is probably justified.

1. Syphilis Study Section, National Institute of Health, U.S. Public Health Service. *J. Amer. med. Ass.* 1948, **136**, 873.
2. Schwemlein, G. X., Bauer, T. J., Craig, R. M., Rodriquez, J., Bundesen, H. N. *Ibid*, **137**, 1209.
3. Willcox, R. R. *Lancet*, 1947, **ii**, 8.

Digitized by Google

McELLIGOTT and his colleagues,[4] at St. Mary's Hospital, Paddington, treated 275 patients for primary or secondary syphilis with 2·4–4 million units of penicillin over seven to twelve days, followed in most cases by 12 injections of neoarsphenamine and of bismuth during six to ten weeks. About half of these patients were followed for twelve months or more, and the remainder for shorter periods. During this time there were 11 cases (4%) in which treatment was known to have failed. Severe toxic effects from the arsenicals occurred in 10 cases. In Montreal MARIN and others[5] treated 201 patients for early syphilis with 2·4 million units of penicillin given in a week, followed by 4 injections a week of 60 mg. of arsphenoxide and 2 injections a week of bismuth during a period of five weeks. Three-quarters of the patients were observed for six months or more. The treatment failed in 9 cases (4·5%), and the outcome seemed doubtful in another 6%. One patient died from arsenical encephalopathy. Both these studies concern too few patients followed for too short a time for definite conclusions to be drawn from the results.

Penicillin has not proved an unmixed blessing for those who treat syphilis. When it is given for the treatment of gonorrhœa in patients who are incubating syphilis the early signs may be delayed or even suppressed. In the same way, the wide use of this remedy for all kinds of infections, major and minor, must mean that syphilis will be masked, and may produce a considerable crop of late syphilitic manifestations in the future.

How Many Nurses?

Mr. JOHN COHEN, PH.D., whose minority report[6] as a member of the Working Party on the Recruitment and Training of Nurses has just appeared, asks us to pause and consider, not how many nurses we would like or think we need, but how many can in fact be obtained from the woman-power of the country. Nor would this give the complete answer: we have to consider, too, how many nurses we can afford. A planned health service, as he points out, "presupposes a planned economy in which a correct proportion of our national resources is devoted to health." As an impoverished country, we must bear in mind that what we spend, however advantageously, on medical services will have to be saved on something else, and we shall have to decide what that is to be. Even if the Treasury were inexhaustible, the supply of women is not. Nursing—like teaching, secretarial work, the social services, the medical auxiliary services, and other occupations open to intelligent women—can only hope to enrol its "fair share" of candidates; and what that fair share may be, he suggests, has never so far been determined. We have yet to discover the optimum number of beds per 1000 of population, and the optimum number of nurses needed to look after them. These things should not be matters of opinion but matters of ascertainable fact.

Pursuing the question whether it is economically justifiable to employ more nurses, Dr. COHEN endeavours to compare the "output" of different hospitals which have different ratios of patients to staff. If it could be shown that patients return to work sooner after treatment in hospitals having relatively large nursing staffs, then we might have evidence that the community could profitably spend more of its resources on employing and training nurses. Arguing that "the task of nurses and doctors alike . . . is, presumably, to speed the patient's recovery" he takes as the economic criterion of nursing (or medical) effectiveness the duration of the patient's stay in hospital. Finding that this is, on the whole, shorter in well-staffed hospitals, he compares the national cost of good staffing with the rational gain in working days saved for production—the evidence providing him with "a prima-facie case, on economic grounds, for substantially increasing the number of trained nurses in general hospitals." Unfortunately, few will agree with the initial assumption on which all this is founded—namely, that the duration of the patient's stay in hospital is a satisfactory "objective measure of the task of nurses and doctors." The length of stay is in fact affected by many variables other than the ratio of staff to patients. Apart from the type of illness (for like groups can be compared with like groups), it may vary with the custom of the hospital, its facilities for investigation and treatment, the pressure of the waiting-list, the provision of convalescent homes, and even the quality of the hospital diet. Nor do the figures he supplies justify Dr. COHEN's prepossession with this particular yardstick.

In 269 voluntary general training hospitals he was able to demonstrate a not very striking inverse relationship between the duration of stay and the ratio of trained nurses to beds. (The figures were taken from surveys made as long ago as 1938.) But this is in fact the only piece of evidence he presents in favour of his hypothesis; and the equivocal results of applying it to other groups of nurses and to doctors should have convinced him that he had lashed himself to the tail of a red herring. Thus the presence of student nurses, in general hospitals, "seems to have little or no effect on the patient's duration of stay," results "offer little support for the view" that the duration of stay could be affected by changing the ratio of doctors to patients; and data from mental hospitals (surveyed in 1934–38) suggest that "an increase in trained nurses alone without increasing the number of other nurses and medical staff is unlikely to reduce patient stay"; whereas an increase of 1·5 untrained nursing assistants per 100 beds (an addition of 800 to our total complement of such assistants) "would apparently reduce stay, on the average, by as much as three months." (The same effect, he believes, might be achieved by adding another 200 part-time doctors to the staffs of our mental hospitals—though an addition to the full-time staff would be likely to have no effect at all.) Faced with all this conflicting evidence Dr. COHEN argues ingeniously that the trained general nurse is more "effective" than the student of general nursing, whereas the nursing assistant is more "effective" than the trained mental nurse; and that full-time doctors in a mental hospital fail to reduce patient stay because they "sometimes tend to persuade some patients to stay on at the hospital so as to improve their condition still more"—an argument which does little to support his hypothesis that the length of patients' stay is a measure of the effectiveness of the doctor.

The fact that this attempt to provide a working measure of nursing production is so questionable does not, however, invalidate Dr. COHEN's general thesis that we are still very ignorant about this subject, and that it is time we studied it more objectively. Since he is concerned only to give an idea of what

4. McElligott, G. L. M., Jefferiss, F. J. G., Willcox, R. R. *Brit. J. ven. Dis.* 1948, 24, 45.
5. Marin, A., Boulais, F. L., Lambert, A., Foisy, J. P., Leclerc, G. *Canad. med. Ass. J.* 1948, 59, 1.
6. Working Party on the Recruitment and Training of Nurses, Minority Report. London: H.M. Stationery Office. 1948. Pp. 78. 1s. 6d.

Digitized by Google

might be attempted he cannot be severely criticised if his example has proved to be ill chosen: he merely reveals the need for fuller study by a team of people in close touch with the subject. But this is long-term policy. Dr. COHEN, like the rest of his colleagues on the Working Party, leaves us with no immediate plan for dealing with the nursing crisis.

Myelomatosis

IN the story of a day in the life of a professor of medicine, broadcast a few weeks ago, the professor was using a sternal bone-marrow smear to diagnose a case of myelomatosis when X rays showed no evidence of the disease. This feat, unusual for any clinician, probably surprised the medical members of the audience more than others, because myelomatosis—or multiple myeloma—calls up a picture of a patient with severe back pains or pathological fractures, in whom X-ray examination reveals typical "punched-out" areas in flat bones and the diaphyses of long bones, and who has Bence-Jones proteose in the urine. The professor, however, was quite right (hardly astonishing since Prof. L. J. WITTS was the author), and he was citing yet another disease in which marrow biopsy has helped to clarify diagnosis and uncover many previously unsuspected cases. For, as LICHTENSTEIN and JAFFE [1] have pointed out, this well-known picture represents the exception rather than the rule. Proper diagnosis of myelomatosis has more than academic interest since there is now some hope of treating and at least arresting the disease.

Before bone-marrow biopsy became widely used myelomatosis was deemed a rare disease. WALLGREN [2] in Sweden could collect only 66 genuine cases between 1873 and 1920; GESCHICKTER and COPELAND [3] at Johns Hopkins found 425 cases in the eighty years before 1929. ROSENTHAL and VOGEL [4] in New York had 3 cases in nineteen years up to 1935; but in less than three years after this date, when marrow biopsy was used, 13 cases were diagnosed. The bone-marrow changes are easily recognised: large numbers of plasma cells of normal and abnormal types are present; the abnormal types have been named by some "myeloma cells," but most agree with DIGGS and SIRRIDGE [5] that all the cells are variants of plasma cells. Now plasma cells can be found in small numbers in almost every marrow smear, but they are increased only in a very few conditions apart from myelomatosis, and in these others the abnormal types do not appear. Armed with this new knowledge it has been possible to diagnose forms that were not thought to be this disease at all. There has also been some simplification; different cellular types of myelomatosis were described, but since marrow biopsy was introduced [6] only one form of myeloma—the plasmacytoma—has appeared. AEGERTER and ROBBINS [7] consider the evidence for distinguishing different forms very doubtful and suggest that the name plasmacytoma is more accurate, and LICHTENSTEIN and JAFFE agree that all forms of myelomatosis are variants of a single disease complex. APITZ [8] is generally credited with the first clear definition of the unity of the various clinical and pathological types of myelomatosis. The most localised form is the "solitary myeloma," in which a tumour appears most commonly in a long bone or a vertebral body and presents either as a tumour or because of a pathological fracture. But a careful search often reveals other small tumours, and in some cases the sternal marrow shows plasmacytosis. The next stage is the classical multiple myeloma with numerous small plasma-cell tumours and a general increase of plasma cells throughout the bone-marrow. The early clinical picture of this type may not suggest bone disease at all. Backache, pains confused with sciatica, or vaguely localised pains dubbed "rheumatism" are common. Other patients may present as a "blood" disease with anæmia, epistaxis, and weakness as the prominent signs; these patients are diagnosed early, as sternal-marrow puncture should be part of the investigation; they also have bone pains, especially backache. Then there is a form in which there is diffuse replacement of hæmopoietic marrow by masses of plasma cells. This generalised form has only been recognised through marrow biopsy; the patients have an insidiously progressive weakness, loss of weight, pyrexia, and anæmia; X-ray films show demineralisation of bone which is often reported as "senile osteoporosis." Finally, there is the rare generalised form in which plasma cells appear in the peripheral blood—the so-called plasma-cell leukæmia. One of the odd features of myelomatosis is its association with amyloid deposits, sometimes only microscopic but sometimes macroscopic and occurring in unusual places. LICHTENSTEIN and JAFFE found amyloid in 10% of their cases, and KOLFF and DHONT have suggested that "primary" amyloid disease (paramyloidosis) may really be an unrecognised form of diffuse myelomatosis; the patients often have Bence-Jones proteinuria and hyperglobulinæmia.

Biochemical changes are often striking in myelomatosis. Bence-Jones proteose in the urine and a rise in serum globulin and serum calcium are the most notable, but none of these is constant or necessary for diagnosis. Bence-Jones proteosuria is absent in many cases; estimates of its incidence vary from 65% to less than 10% of cases. GUTMAN [9] says that serum calcium is raised in 30–50% and serum proteins in over 50% of patients; renal obstruction may raise the serum inorganic phosphate. These changes are not correlated, for a patient may have a high serum protein but no Bence-Jones proteosuria, and so on. The diagnosis of myelomatosis, when X-ray findings are not clear, consequently depends more on sternal-marrow biopsy than on any other investigation. When the physician is faced with a patient aged between 40 and 60 years with pyrexia of undetected origin wasting, backache, and possibly anæmia and epistaxis, myelomatosis should be kept in mind and looked for.

Treatment of myelomatosis with stilbamidine (4, 4-diamidinostilbene) was first reported by SNAPPER in New York in 1946. Stilbamidine was designed for the treatment of kala-azar, and, because in this disease the serum globulin is high, it was thought

1. Lichtenstein, L., Jaffe, H. L. *Arch. Path.* 1947, **44**, 207.
2. Wallgren, A. Untersuchungen über die Myelomkrankheit. Uppsala, 1920.
3. Geschickter, C. F., Copeland, M. M. *Arch. Surg.* 1928, **16**, 807.
4. Rosenthal, N., Vogel, P. *J. Mt Sinai Hosp.* 1938, **4**, 1001.
5. Diggs, L. W., Sirridge, M. S. *J. Lab. clin. Med.* 1947, **32**, 167.
6. Kolff, W. J., Dhont, J. *Amer. J. med. Sci.* 1948, **215**, 405.
7. Aegerter, E., Robbins, R. *Ibid*, 1947, **213**, 282.
8. Apitz, K. *Virchows Arch.* 1940, **306**, 631.
9. Gutman, A. B. *Bull. N.Y. Acad. Med.* 1947, **23**, 512.

Digitized by Google

that the drug might have some effect in myelomatosis which is also characterised by disturbance in plasma proteins. SNAPPER [10] has recently reviewed his results on 35 patients. The drug is given intravenously and a course of 15–20 injections of 150 mg. is needed. The doses are given daily unless there is renal damage when they are spaced out to twice a week. The diet has to be controlled and animal protein kept to a minimum. A troublesome side-effect is a dissociated anæsthesia in the area distribution of the trigeminal nerve, which often appears one to three months after the course of treatment. SNAPPER estimates that in four-fifths of his patients bone pains were relieved and the disease arrested; "arrest" is the correct term, for X-ray changes remain stationary and serum protein may remain high. Most of his patients relapsed within a year and did not respond so well to second courses of stilbamidine. Of the 12 patients who had been under observation for more than a year after treatment, 4 had died and 5 were classed as satisfactory and were ambulant; 5 of the 8 survivors had lived for three years since diagnosis and one for six years. SNAPPER and his co-workers showed that in patients with biochemical evidence of disturbed protein metabolism basophil bodies appeared in the cytoplasm of the marrow plasma cells when the stilbamidine dose had reached about 1000 mg. Histochemical and spectrophotometric studies suggest that these bodies are composed of ribonucleic acid and stilbamidine. SNAPPER suggests that the myeloma cells contain abnormal nucleoproteins in their cytoplasm, and that stilbamidine has a specific affinity for them. Stilbamidine is far from the ideal therapeutic agent for myelomatosis, for its action is only partial and it has unpleasant side-effects, but groundwork for experiment has been laid by SNAPPER and we must hope that more effective compounds will be discovered. If the apparently solitary myelomas are really part of a generalised disease, then the present treatment by surgical removal and subsequent local radiotherapy might appear wrong. GOOTNICK [11] has noted that there are few survivors after ten years. But in practice there have been many reports of survival for some years without evidence of general spread, and operation may be needed to relieve mechanical disability. Perhaps evidence of extensive spread in the sternal marrow should be a contra-indication for operation.

Here then is another condition in which improved diagnostic methods have made earlier diagnosis possible, for which effective therapy is being developed, and which is passing over from the surgeon's to the physician's care.

10. Snapper, I. *J. Amer. med. Ass.* 1948, **137**, 513.

11. Gootnick, L. T. *Radiology*, 1945, **45**, 385.

Annotations

PRIVATE PATIENTS NOT ADMITTED

IN a speech reported on p. 515 Mr. Bevan expressed great satisfaction at the fact that 92–93% of the population of Great Britain have already chosen their doctor in the National Health Service, and said that signatures are still coming in at the rate of 150,000 a week. Enrolment has indeed been far speedier than was expected. In view of the general reluctance to fill in forms of application for licences, ration books, and the like, it would not have been surprising if many more people had put off choosing a doctor, or joining his list, until the onset of illness made this imperative. Even if the rate of new entrants falls steadily from now onwards, it is very likely that by the time the winter illnesses have come and gone no more than 1 in 40 or 50 will remain outside the general-practitioner service.

This bears out our contention of a fortnight ago that the number of people who might wish to attend health centres as private patients will be very small. Some private patients will be under the care of doctors who have not taken service under the Act; others will have elected to remain private patients specifically to avoid ever going to see their doctor; not a few will be elderly people, many of whom are reluctant to change their habit pattern or to risk any alteration in their lifelong relationship with their doctor. When all such are excluded we are left with an almost negligible proportion of patients who while remaining private might want to pay an occasional visit to the health centre. On an average through the country this proportion is scarcely likely to be as high as 1% (or 40 patients among the 4000 of a fully extended practitioner). Though there will of course be areas with abnormally large numbers of private patients, these will seldom be the ones first chosen to have health centres.

Nevertheless it seems that the Minister remains convinced, as a matter of principle, that private patients must be excluded from the use of health centres—even if this ruling means that the construction of some of the projected centres will be halted. In this he is supported by Mr. Somerville Hastings. The *Times* on Sept. 10 said:

> "The doctors have been told that they must not see private patients at a health centre provided by the local authority. This is a blunder. Specialists are to be allowed to carry on private practice at State-provided hospitals; yet general practitioners are to be denied similar privileges at State-provided health centres. All private patients are perfectly eligible to benefit from the facilities of the health service and, as taxpayers, they are part-owners of the buildings in which the work of the service is done. Why should they not pay for what in any case they are entitled to get free?"

Mr. Hastings on Sept. 15 replied that if the private patients "are intelligent people, they would only ask to be seen privately and pay for it if they expected to receive either preferential, more considerate, or better treatment. And this is what they would be bound to get, so that there would be two standards of treatment in the same health centre." But is this theoretical reasoning supported by experience? In actual fact people who have elected to remain private patients still seem to be content to attend for some services at their doctor's surgeries, and ask there no preferential attention, nor any more considerate or better treatment than that being given to his State-enrolled patients. The truth seems to be that the great majority of patients remaining as private patients do so in order that they may suit their own convenience as to when, where, and how often, they consult their doctor. For certain services (e.g., recurrent injections, minor dressings, vaccinations, ear syringing, the renewal of priority certificates, or the obtaining of signatures for passports and other documents) it generally suits private patients to come at a fixed, and early, time to their doctor rather than wait indefinitely at home for his arrival. Why should they not seek similar services in a health centre? No more than now will they need or ask any special attention.

If a doctor had any substantial number of private patients, the fact that these were denied entry to the health centre might in the end prove prejudicial to his

Digitized by Google

public practice, however good his intentions. He might be obliged to hold a surgery at his own home before proceeding each morning to the centre, and this might easily cause a waste of time through which his day's work would suffer.

Mr. Hastings very rightly wants to avoid two standards of treatment inside the health centre. But by excluding the private patient is he not in danger of fostering the idea that something better, or something more considerate, can be provided for the private patient at the doctor's own surgery? Surely our aim is to provide the best possible conditions for practice inside the health centres. We want this to be recognised alike by doctor and patient. We shall not teach any patient the value of health centres by denying him entry to them. We shall not enhance the attraction nor increase the efficiency of the centre by carving on its lintel "No admittance for Private Patients." Once the centres are provided, we must use them to their greatest advantage—use them especially to save the doctor waste of time and effort so that his energies may be utilised to the full. The Act allows the patient the right to obtain privately any section he chooses of his medical care, and expressly permits the practitioner to give private attention to patients who insist on having it. Anomalies are bound to arise through this very provision. But the more we try to keep separate the care of the two groups of patient, the greater the difficulties we create for ourselves and the greater the waste of man-hours we cause. In any case we could not carry the separation to a logical end without arriving at a ludicrous conclusion. If we exclude the private patient from the centre in person, must we also prevent his doctor from testing in the centre his blood, his urine, or anything that is his? Must telephone calls to the doctor be refused at the centre if they concern private patients? Indeed, may the doctor even ponder the problems of a private patient, or discuss them with a colleague, once he is inside the portals of the centre? Each and every one of these things he can do, or have done, for his patient at the State-provided hospital: why not at the State-provided centre?

Feeling, as we do, that there is no logical or justly calculable point at which a line of division could be drawn, and confident that numerically the demands made on the centre by the private patient will not be great and will not in practice necessitate any discrimination between the two types of patient, we still believe that in the first experimental centres doctors should not be forbidden to treat those private patients who elect to attend there. The day-to-day experience of these centres will be far more valuable than any present postulation; and, if our contentions are proved wrong, and the smooth running of these early centres founders on the rock of class discrimination, it will then be time enough to try instead the feasibility of making the doctor segregate his patients and conduct his practice in duplicate from two separate establishments. Time enough, if our present opportunity has not itself been lost through disagreement, discouragement, and delay.

RADIOACTIVE PENICILLIN

THE prospect of growing supplies of radioactive isotopes, announced in these columns last week (p. 469), opens up an exciting and obviously fertile field for pharmacological and physiological research. It is 25 years since Hevesy [1] first applied isotopes to the study of plants, using radioactive lead. In the early experiments only naturally occurring radioactive substances could be used and the scope of this powerful weapon of investigation remained strictly limited until a method for producing radioactive isotopes artificially was discovered by Joliot-Curie and Joliot [2] in 1934. In 1932, Urey and his colleagues discovered deuterium (H^2) and soon developed practical methods for the production of highly concentrated "heavy water." In the next decade radioactive isotopes of nitrogen, carbon, sulphur, phosphorus, iron, and many other elements were produced. In a relatively short time, therefore, a wealth of isotopic tools became available for the elucidation of physiological and biochemical problems which had previously defied solution. Much interesting information was soon gathered. Using radioactive sulphur, for instance, Tarver and Schmidt [3] showed that in normal metabolism the sulphur of cystine is derived, at least in part, from methionine, but not from elementary sulphur or from sulphate. Radioactive isotopes of iron have been used by Whipple and his associates [4] in biochemical and physiological studies of erythrocytes. A fascinating aspect of isotope research is the determination of the steps in the breakdown or synthesis of biologically important products by the organism. An isotope of phosphorus, P^{32}, has been used for the study of phospholipid, nucleoprotein, and carbohydrate metabolism, while thyroid function and iodine metabolism, including the rôle of the pituitary thyrotropic hormone, have been studied with I^{131}.

Thus, starting from naturally occurring radioactive lead, through the induced radioactive isotopes of many elements, organic substances have been built up containing radioactive carbon, nitrogen, phosphorus, or sulphur, and these have provided us with agents for probing the mysteries of intermediate metabolic processes in biological systems. The latest application of this technique is in penicillin research, where the mould is made to incorporate a sulphur isotope into the penicillin molecule. Rowley and colleagues,[5] while investigating the glutamic-acid uptake by bacteria, used a preparation of radioactive penicillin, made by inoculating a synthetic broth medium containing S^{35} with a vegetative culture of the Q176 strain of *P. chrysogenum*, in which the sulphur content had been reduced to a point at which it became the limiting factor in the yield of penicillin. The yield from 2 ml. of broth was 250 I.U., representing a 12% conversion of the sulphur in the broth into penicillin with a specific activity of 0·05 microcurie per I.U. It was noted that the presence in the medium of 50 millicuries of S^{35} per litre did not adversely affect the growth of the mould. A preparation of radioactive penicillin with a much weaker activity has recently been reported [6] from the United States. With their radioactive penicillin Rowley et al. demonstrated that the absorption of penicillin, if any, probably amounts to less than 10 molecules per bacterium (*Staph. aureus*).

Extending this work on penicillin labelled with S^{35}, Rowlands, Rowley, and Stewart, in this issue, report some excretion and absorption studies in cats. By giving mixed ordinary and labelled penicillin intramuscularly they found that 100% of the radioactive sulphur isotope was excreted in the urine, but the recovery of biologically active penicillin was much less. There was no evidence of any retention in the body, as the radioactive breakdown products (at present unknown) were excreted over the same interval of time as the penicillin itself. In a previous study of the absorption of penicillin given by mouth, Stewart and May [7] concluded that "the most important factor influencing the absorption of penicillin seems to be the unexplained

1. Hevesy, G. *Biochem. J.* 1923, **17**, 439.

2. Joliot-Curie, I., Joliot, F. *C.R. Acad. Sci., Paris*, 1934, **198**, 254.
3. Tarver, H., Schmidt, C. L. A. *J. biol. Chem.* 1939, **130**, 67.
4. Hahn, P. F., Balfour, W. M., Ross, J. F., Bale, W. F., Whipple, G. H. *Science*, 1941, **93**, 87.
5. Rowley, D., Miller, J., Rowlands, S., Lester-Smith, E. *Nature, Lond.* 1948, **161**, 1009.
6. Howell, S. F., Thayer, J. D., Labaw, L. W. *Science*, 1948, **107**, 299.
7. Stewart, H. C., May, J. R. *Lancet*, 1947, **ii**, 857.

Digitized by Google

individual variations in the absorptive capacity of the gut." Stewart and his colleagues have now produced evidence supporting their previous contention. When the radioactive penicillin was given to cats by mouth, the urinary excretion of radioactivity was no longer complete as when the penicillin was given intramuscularly, but was reduced to 54–24% of the initial dose, while the proportion of biologically active penicillin excreted in the urine was even considerably less than this. In one cat only 24% of the original radioactivity had appeared in the urine, and as much as 59% was unabsorbed, being recoverable from the gut contents post mortem. In this case urinary excretion had not ended, but the presence of such a large percentage of the original activity in the gut after six hours strongly suggests that non-absorption from the gut is the reason for the low urinary excretions after oral penicillin. It seems, then, that attempts to improve the absorption by this route are still worth while.

MEMORANDUM ON RH FACTORS

THE doctor who studies recent reviews and pronouncements on the Rh factor may well despair of ever understanding this example of what Lord Samuel calls "the unceasing elaboration of human knowledge"; the rows of rival symbols, the genetic terminology, the "blocking" antibodies, all combine to bewilder him. Yet for the sake of his patients he must understand the practical application of this new knowledge. He will be greatly helped by the brief, informative, and inexpensive summary published this week by the Medical Research Council.[1] Without shirking descriptions of the more difficult points, this memorandum presents a clear picture of the clinical consequences of neglecting the Rh factors, and it puts subjects like the Rh subgroups and the peculiarities of Rh antibodies into their proper perspective.

After a very short historical introduction, the first section, by R. R. Race, describes briefly the various Rh groups. He points out that 95% of all dangers due to Rh blood-groups are due to the original Rh group now known as D and its antibody anti-D, and he quotes the latest figures showing that in England 83·2% of the population are Rh-positive (D-positive) and 16·8% Rh-negative. There follows a brief but thorough description of the Rh subgroups and their genetic relationship according to the ideas of R. A. Fisher. Race rightly says that anyone who makes the effort necessary to master these groups has, at the same time, achieved at least an elementary knowledge of human genetics in general. In describing the Rh antibodies the term "blocking" antibodies is dropped, since it is not clear that this is, in fact, the action of these antibodies. What is known is that anti-D, the commonest Rh antibody, exists in two forms; one form will agglutinate red cells containing the antigen D (D-positive cells) when these cells are suspended in saline solution, whereas the other will agglutinate them only if they are suspended in a protein medium—best results are obtained with 20% bovine albumin. Cells exposed first to this albumin anti-D will not subsequently be agglutinated by the saline antibody; hence the term "blocking" or incomplete antibody. But when Diamond gave intravenous injections of Rh-positive blood to Rh-negative male volunteers, he found that the saline agglutinins appeared first, and that then with repeated doses they diminished and eventually completely disappeared, being replaced by a rising titre of the antibodies detectable only in albumin suspension. Diamond therefore regards the albumin antibodies as "hyperimmune agglutinins." The authors of the M.R.C. memorandum adopt the noncommittal but descriptive terms "saline" and "albumin" agglutinins or antibodies.

In the second section P. L. Mollison deals with clinical considerations and covers more familiar ground. He details how immunisation to Rh can be produced by transfusion of Rh-positive blood into Rh-negative persons or by a pregnant Rh-negative woman having a Rh-positive fœtus. A less well-known fact is that the intramuscular injection of blood—e.g., for eczema—can produce life-long immunisation. Mollison emphasises the importance of detecting Rh antibodies in the mother's blood, since this is the best indication that the infant may be affected by hæmolytic disease. Two examinations should be made, one early in pregnancy and one about six weeks before the expected date of delivery; the first examination reveals sensitisation produced before pregnancy, since antibody developing for the first time during a pregnancy rarely shows before the fifth month. The clinical pictures of hæmolytic disease and of the allied syndromes are described, and the various means of dealing with the situation and the question of advising parents about future pregnancies are fully discussed. The technical details of exchange transfusion provide useful practical points for workers in maternity hospitals.

Clinical laboratories are not at present encouraged to undertake Rh testing, and the regional transfusion laboratories do most of this work. However, some clinical pathologists may be interested in doing their own, especially if they are in situations distant from the regional centres. They will obtain comprehensive help from the third section, in which A. E. Mourant fully sets out the practical details of Rh testing. Altogether this is a highly valuable and authoritative addition to the M.R.C. series of White Memoranda.

1. The Rh Blood Groups and their Clinical Effects. By P. L. Mollison, A. E. Mourant, R. R. Race. M.R.C. Memo. no. 19. H.M. Stationery Office. 1948. Pp. 74. 1s. 6d.

THE ARTIFICIAL HEART

ATTEMPTS have been made since the turn of the century to devise a machine which would perform the circulatory duties of the heart. Twenty years ago Dale and Schuster [1] showed that this could be done, and the perfusion pump that they devised and demonstrated at University College, London, is still in use. But when, in addition, physiologists sought to oxygenate the blood mechanically outside the body, the task became much more complicated. So far the only fully efficient oxygenator has been the isolated lungs. Some of the earlier attempts at artificial oxygenation now seem rather crude; hydrogen peroxide and oxygen have been injected into the blood-stream, while oxygen-carrying solutions of various kinds have been tried. The intravenous injection of oxygen, unless performed very slowly, carries a severe risk of embolism. A different type of experiment followed the demonstration by Hartridge and Roughton that hæmoglobin would take up oxygen much more readily in solution than when enclosed in the red cells. But as would be expected, animals perfused with solutions of hæmoglobin rapidly died as the hæmoglobin passed into the urine and lymph. Further attempts were based on the principle adopted by nature in the lungs—the exposure of a thin film of red cells of large surface area to oxygen. Perhaps the most outstanding experiments were those by Bayliss and his co-workers [2] and later by Daly,[3] but neither of their thin-film methods was suitable for maintaining an animal for long.

The recent advances in intracardiac surgery have stimulated renewed interest in cardiopulmonary machines. In this issue Dr. Björk describes one which has been evolved in Professor Crafoord's clinic

1. Dale, H. H., Schuster, E. H. J. *J. Physiol.* 1928, 64, 356.
2. Bayliss, L. E., Fee, A. R., Ogden, E. *Ibid*, 1938, 66, 443.
3. Daly, I. de B., Thorpe, W. V. *Ibid*, 1933, 79, 199.

Digitized by Google

at the Sabbatsberg Hospital in Stockholm. The superiority of this machine lies in the excellent oxygenation which is obtained by spinning a row of plates which dip into a trough of blood, and so expose constantly changing thin films of red cells to oxygen (or anæsthetic gases if required). On the mechanical side the machine owes much to the work of Andersson, who was also responsible for the engineering aspects of the spiropulsator, which Professor Crafoord uses so successfully for giving anæsthetics during thoracic operations. The oxygen uptake of the blood in Björk's apparatus is much better than in any previous machines, as much as 110 ml. of oxygen being added to each litre of blood per minute. Heparin is added to prevent clotting, but careful filtration of the blood returning to the animal is essential to avoid embolic complications. There is a considerable breakdown of red cells in such a machine, but it has been elaborated sufficiently to maintain the oxygen requirements of the brain of a dog for half an hour. It is known that the aorta can be clamped distally to the left subclavian artery for half an hour without any significant damage to the lower half of an animal, and thus by clamping the venæ cavæ the heart can be opened relatively bloodlessly.

The aim of these experiments is to isolate the human heart from the circulation while it is opened for operative procedures. This new work is a great step forward, but it leaves us a long way from this goal. This year an alternative approach has been exploited by Holmes Sellors [4] and Brock [5] in their operation for the relief of pulmonary stenosis. Both have successfully thrust an instrument through the wall of the right ventricle and divided the constricting diaphragm in the beating heart.

VETERINARY PROGRESS

THE annual congress of the National Veterinary Medical Association, held at Southport from Sept. 8 to 15, once again illustrated the similarity between veterinary and human medicine in the urgent problems of the moment. Tuberculosis, virus diseases, and salmonella infections are all exercising the minds of those responsible for the control of communicable diseases, whether in animals or in man. Prof. T. Dalling, who became Chief Veterinary Officer in August, discussing the control of tuberculosis in cattle, emphasised that one of the chief difficulties in tuberculin-testing is the non-specific sensitisation to mammalian tuberculin. Steps are being taken to increase the specificity of the comparative intradermal test, in which avian and mammalian tuberculins are injected simultaneously at different sites and the reactions compared. Extensive experiments done on the specificity factors of P.P.D. tuberculins produced from different acid-fast bacteria have shown that twice as much avian P.P.D. is required to elicit the same reaction in bovine sensitisations as in human; Green suggests that for this reason bovine P.P.D. might be more useful in the comparative test for distinguishing between specific and non-specific infections in cattle. Work is also being done on the chemical modification of tuberculins. In a large-scale field experiment the double intradermal test as usually carried out proved to have no advantages, but workers in Northern Ireland have shown that 7 days after the injection of tuberculin the site of injection develops an enhanced specific sensitivity. Less laborious and more precise methods of detecting bovine tuberculous infection in cattle may arise from this work, but already the adoption of the single as opposed to the double intradermal tuberculin test has greatly increased the amount of testing that can be performed. Professor Dalling urged the importance of suitable callipers for measuring skin thickness, and now that these are obtainable they should be widely used by the Ministry's whole-time and part-time staff. There are now over a million cattle, or 13·9% of the total cattle population, in attested herds and 250,000 in herds licensed to produce T.T. milk, but various speakers demanded a more vigorous policy of eradication.

The salmonella organisms responsible for bacillary white diarrhœa in poultry and fowl typhoid seldom cause disease in man, but various new salmonella types which may cause food-poisoning in man have lately been isolated from fowls, eggs, and animals. It has been shown, too, that salmonella infection in cows and calves is commoner than was generally realised.[1] In poultry, salmonella infections call for an organised programme of agglutination-testing and attention to incubator hygiene. Incubator infection is the chief method of spread through setting eggs, the shells of which are infected by fæcal contamination. Mr. J. E. Wilson, who discussed the control of these infections, described the technique of incubator fumigation in detail; to forestall shell penetration it should be carried out as soon as possible after setting. In large outbreaks he recommended sulphonamide therapy in conjunction with other measures. Organisms which are sensitive to sulphonamides, or to one of the antibiotics, will of course be equally so, whether they are infecting man, animals, or birds; but the behaviour of the antibacterial drugs differs considerably in different species owing to variations in absorption and excretion. Thus Mr. J. Berger and Mr. J. Francis showed that, in domestic animals, 'Sulphamezathine' gives consistently higher blood-levels than equal doses of sulphadiazine; whereas in man the reverse is true.[2]

Mr. Horace Thornton, chief veterinary inspector, Newcastle-on-Tyne, contended that the standards of meat hygiene, inspection, and control are much lower in Britain than in Continental and other countries where the veterinary profession has taken a greater part in the work. He advocated routine bacteriological examinations in the inspection of borderline carcases and a greater use of biochemical tests. The adoption of such methods would result in the release of many of the carcases which, in Britain, are now totally condemned. The criteria now applied in Germany in relation to tuberculous carcases deserve critical study. Some of his specific criticisms are set out by Mr. R. F. Montgomerie, PH.D., the association's president, in our correspondence columns. With regard to home-killed meat, however, Mr. Harry Priestley [3] says there is no cause for alarm. It is a pity that animals are rarely inspected before slaughter in Britain, although many diseases which are difficult to detect in the dead animal can readily be diagnosed in life. Several speakers regretted that the Ministry of Food has not regularised the slaughter of horses for food.

Encephalitis is as complicated a subject in dogs [4] as in man. Mr. A. B. MacIntyre, Dr. D. J. Trevan, and Dr. Montgomerie showed that apart from dietary and miscellaneous causes canine encephalitis is sometimes associated with canine distemper and with a newly recognised virus infection which causes a characteristic thickening of the pad epithelium.

On Sept. 10 the association visited Liverpool University and its Veterinary Field Station, where Prof. J. G. Wright described the techniques for cæsarean section in the cow. In his view the incision should be made just to the left of the midline, and not in the right flank. Despite the weight of the abdominal contents he has not been troubled by postoperative rupture.

4. Sellors, T. H. *Lancet*, 1948, i, 988.
5. Brock, R. C. *Brit. med. J.* 1948, i, 1121.

1. Field, H. I. *Vet. J.* 1948, **104**, 251.
2. See *Vet. Rec.* 1947, **59**, 131; *Vet. J.* 1947, **103**, 193.
3. *Manchester Guardian*, Sept. 18, p. 4.
4. Parry, H. B. *Vet. Rec.* 1948, **60**, 389.

Digitized by Google

INTERNATIONAL CONGRESS OF INDUSTRIAL MEDICINE

LAST week we briefly described the opening meeting at which Lord Moran, P.R.C.P., presided and the 900 delegates from more than forty countries were welcomed by Mr. George Isaacs, Minister of Labour, and by Mr. T. E. A. Stowell, F.R.C.S., first British president of the Commission Internationale Permanente pour la Médecine du Travail. Mr. Stowell paid a special tribute to the work of Prof. L. Carozzi, who was responsible for forming the commission in Milan in 1906 and has been its secretary-general ever since.

The following report describes some of the many sessions held from Sept. 13 to 17. At a crowded final session Lord Webb-Johnson, P.R.C.S., presided, and Mr. G. R. Strauss, Minister of Supply, gave the closing address. Prof. P. Mazel expressed the thanks of the delegates for the hospitality of the British Council, and said that the health and happiness of the workers in this country is an expression of national well-being and an achievement of which industrial medical officers, nurses, managers, and others working in industry may well be proud.

Social events included a big Government reception at Lancaster House on Tuesday, and a reception by the Royal College of Physicians on Friday evening. On the same day Mr. H. E. Griffiths delivered at B.M.A. House the Mackenzie industrial health lecture, entitled The Surgeon in Industry. During the present week the visitors, in small groups, have been visiting laboratories, institutions, training centres, and industrial undertakings of many kinds in England, Wales, and South-west Scotland.

The Law

A session on the industrial medical content of the law produced a vigorous discussion. After Mr. MOELWYN HUGHES, K.C., and Dr. P. PRINGLE had described the English law relating to industrial medicine and compensation, Prof. L. CAROZZI (Italy), the chairman, dealt with current industrial legislation in other countries. Everywhere, he said, the application of labour legislation meets with difficulties, as shown in the reservations made by the committee of experts of the International Labour Organisation on the application of conventions. It needs good will on the part of governments, employers, and workers to attain the aim of such legislation, which is the common good and the team spirit. He thought that laws relating to health and hygiene should be revised and codified; often the regulations are too numerous and sometimes they are contradictory. Today social-security laws tend to embrace both compensation and the prevention of accidents and industrial diseases, a state of affairs which makes the application of industrial legislation more complicated. In fact the medical supervision and prevention programmes allotted to social-security departments encroach on the rights and duties of the technical and medical factory inspector and of the works medical officer. Though the legislators envisage a permanent liaison between the two functions, the methods adopted are not satisfactory. He instanced the difficulty which French workers encounter in obtaining compensation, because industrial diseases have been too precisely defined; the social-insurance department has plenty of money which is not distributed in compensation as it ought to be.

Dr. I. URBANDT (Argentine) read a paper on the regulation of hygiene and safety in factories, and Dr. CATHERINE SWANSTON reviewed the protective legislation for women and young persons in industry. She said that the factory inspectorate, established in 1833, is responsible for much reform of the hours of work of women and young persons, but even now the law as it stands in relation to their employment is in many respects out of date, illogical, and uneven in its application.

One of the main points arising in the discussion was whether compensation laws should be general, with details in more flexible codes, or whether the compensatable illnesses or accidents should be precisely defined and scheduled as in the French and in a lesser degree in the English law. Some speakers feared that if the compensation laws were interpreted in a flexible manner the workers might exploit the compensation funds, but others saw little risk of this provided careful medical examination establishes that the morbid conditions are directly due to the occupation.

Organisation of Industrial Medical Services

Prof. P. MAZEL (France) reviewed the organisation of industrial medicine in France and pointed out that by a law passed in October, 1946, all establishments, societies, and associations employing paid workers, whatever their number, must arrange for medical services for the workers. Any registered doctor may be chosen by an employer or industrial committee to carry out the duties, his payment being made at a standard rate by the employer. The doctors' duties consist in the examination of applicants on engagement and also the periodical medical examination of all workers at least once a year, and more often when the worker is under 18 years of age or engaged in dangerous work. Dr. Mazel also described the administration of this service, which is in effect a national industrial medical service.

Dr. L. GREENBURG (U.S.A.) discussed the industrial health services in New York State, where there are 52,000 factories in which nearly 2 million workers are employed. Supervisory work is in charge of the Department of Labour and is carried out by a factory inspection service and by the division of industrial hygiene and safety standards. The licensing of industrial medical bureaux and of physicians for industrial practice is vested in the workmen's compensation board of the State. This board is also in charge of the adjudication of compensation claims for industrial injuries and occupational diseases. Labour unions, by establishing clinics, by including health provisions in labour contracts, and by programmes of health education, greatly strengthen the movement for improved health among workers. Voluntary health agencies also play a part. The United States Public Health Service, through the division of industrial hygiene, has conducted research, has aided State units in the conduct of their work, and has provided funds and personnel for developing industrial medicine.

Dr. A. BRUUSGAARD spoke on the industrial medical services in Norway, which cover 17% of the employees in industry, commerce, and transport (exclusive of shipping).

Almost all firms of more than 500 employees are covered, and a fifth of all firms with more than 50 employees now have a medical service. The scheme has been set up by a voluntary agreement between the Norwegian Federation of Labour, the Employers' Association, and the Norwegian Medical Association. This voluntary aspect is regarded as of the utmost importance, to ensure the development of a democratic system.

Dr. A. NYYSSÖNEN gave an account of the industrial health service in Finland, and Dr. N. L. LLOYD described the organisation of the British Ministry of Supply medical service.

Digitized by Google

Medical Supervision in Industry

Dr. H. A. DE BOER, of the International Labour Office, said that international conventions are a stimulus to national legislation. Before the Medical Examination of Seafarers Convention in 1921, only six countries had legislation protecting seamen, but the convention caused nearly all countries to adopt protective legislation.

Medical supervision of the worker is being developed in many countries, and in most of Europe and in the U.S.A. it has reached a high level of efficiency. The difficulties of the pioneer in industrial medicine in Western countries have been slight, however, as Dr. H. P. DASTUR showed, compared with those now being experienced by the few men and women interested in industrial medicine and nursing in countries like India, with their racial differences and illiteracy.

In European countries perhaps the greatest remaining difficulty is the discontinuity in the medical services for workers at different ages. Most of them have established school medical services, but these still need to be integrated as part of the child's school life and continued through the years of adolescence in industry and commerce. The vast amount of non-absent morbidity among adolescents is seldom realised.

Dr. W. G. DONALD (U.S.A.) gave an account of the University of California's student health service, which is on a lavish scale. If the American adolescent coming from privileged homes is in such need of help, the European adolescent coming from less privileged homes and earning his living must need much more. Here is one of the opportunities of the county colleges, which, under the Education Act, 1944, will shortly be established compulsorily in Great Britain. Adolescents dispersed in a large number of small factories will, for one day a week, be collected into a functional group which could be subject to guidance and medical supervision. Mr. F. W. COE, headmaster of a day continuation school, laid great emphasis on the fact that if "black-coated workers are not to be superior to black-handed workers" both the schoolmaster and the doctor have a great part to play in building up group morale. Elaborate schemes for the examination and treatment of adolescents are of little importance compared with the feeling that the doctor and nurse, working either in industry or in a county college, are part of the adolescent's life.

Incentives, Job Adjustment, and Absenteeism

Prof. ELTON MAYO (U.S.A.), in a paper read by his daughter, pointed out that labour is more than a number of individuals collected together. The great significance of the Hawthorne experiment and subsequent experience is that economists and others have failed to grasp the effect of group influences on the individual. The individual worker is a member of a team, and statistical studies on the frequency of absence show that the largest class is composed of those who have not been absent at all.

Dr. T. M. LING traced the effect of psychological causes arising within the individual, which help or hinder his adjustment to a social group. In a later discussion several speakers supported Dr. Ling's plea for closer and more extensive study of personality variations.

Dr. F. R. GRIFFIN dealt with the problem of morale, particularly in small factories. Morale cannot be considered as an isolated factor, for it is one that arises from the total situation.

Dr. OSWALD SAVAGE's paper, though limited to the discussion of rheumatism as a cause of industrial disability, reminded delegates, who up to now had been considering psychological or psychosomatic causes of absenteeism, that a large amount of disability is caused by organic diseases, particularly those of a chronic nature.

Other speakers gave accounts of their personal experiences and methods they have adopted to reduce absenteeism. The very good results they claimed were generally felt to be a tribute to their enthusiasm rather than to the particular methods.

Work and Skill

The discussion on this subject showed a big difference in the Continental and British approach. The former, very similar to the American, places emphasis on job analysis integrated with personality profiles; the latter approaches human relationships in industry from a sociological and anthropological point of view. The British regard the promotion and maintenance of morale as of greater importance than the technical efficiency of the worker, with or without a machine.

Sir FREDERIC BARTLETT described the development of skill, which consists in a sequence of responses subject to psychophysical or mental control and which sets out to achieve an object. The most promising approach to an understanding of practical mental skill lies in a controlled study of the conditions, both individual and social, which lead to the formulation of programmes, and of how these can be revised and altered and yet kept in touch with rapidly changing circumstances. As Mr. P. A. D. GARDNER and subsequent speakers emphasised, physical skill reaches its highest form in craftsmanship.

Dr. A. T. M. WILSON urged that doctors working in industry should be better trained to integrate the contributions of workers in other fields of social sciences.

Health and Disability

Against the background of Dr. G. E. GODBER's description of the National Health Service, delegates discussed the development of health clinics in industry and the part that medical supervision plays in the successful employment of the limited or disabled employee.

Dr. F. E. POOLE (U.S.A.) spoke of the need to emphasise not the disability but the ability of each patient: the whole personality, rather than a specific disease or disability, has to be assessed, expressed in simple terms, and related to a flexible system of job classification. The importance of this was apparent in Prof. TOM FERGUSON's account in the employment of disabled persons in Hillington. Details such as lavatories with hand-grasps for use by men without legs are important if disabled men are to feel personal independence within the factory. The success of such experiments is to be judged with the regularity of attendance (at Hillington only 5·7% of working days are lost from all causes of absence), economic production, and the development of social and extra-industry interests among members of the group. The fact that a factory is an economic success is important from the purely productive point of view, but more important because of the feeling of usefulness it gives to disabled persons.

Dr. LOGAN thought that many of the systems of estimation and classification of disablement place too much emphasis on surgical disabilities: in view of the large numbers of persons suffering from peptic ulcers, chronic bronchitis, and degenerative conditions, more attention should be paid to the medical aspects of disablement.

Dr. L. ROCHE (France) in the closing paper, emphasised that production can be considered an index of health and well-being in its widest aspects.

Hazards of Particular Industries

Dr. J. GREGORY, who read Dr. GEORGE FLETCHER's paper and amplified his remarks on byssinosis in cotton workers, pointed to the need for studying the early development of pulmonary symptoms among such workers.

Digitized by Google

The risk of boot and shoe operatives catching tuberculosis depends on the spacing of workers on a factory floor; but Dr. ALICE STEWART's findings, which confirm the presence of a high incidence of tuberculosis in the Northampton boot and shoe trade, show the necessity for further investigations in other industries and more work on the epidemiology of tuberculosis.

Dr. PATRICIA SHAW pointed out that the gross mortality figures of shop assistants do not differ—except in specific instances, such as grocers—from those of the general public. A significant fact is the disappearance of men of the age of 30 and onwards from the distributive trades. She would like to think that this is because shop assistants become proprietors; but experience shows that this is not so. Probably, because of the frustrating nature of their work, shop assistants drift into other occupations. Much more study is required to decide simple problems such as whether the incidence of varicose veins is higher in shop assistants, who stand all day, than in other occupational groups.

Occupational Tumours of the Bladder

Prof. G. H. GEHRMANN (U.S.A.) described experiments on dogs confirming other work on the carcinogenic action of beta-naphthylamine; but no tumours could be produced with aniline, benzidine, and purified alpha-naphthylamine. Dr. G. M. BONSER spoke of her experiments on the induction of tumours with beta-naphthylamine, and confirmed hitherto uncovered results with the other amines. Prof. G. DI MAIO (Italy) from a considerable experience of these tumours, gave an account of the clinical and cystoscopic appearances, the highest incidence being among benzidine and alpha- and beta-naphthylamine workers. Prof. E. C. VIGLIANI and Dr. M. BARSOTTI (Italy) presented the results of observations among chemical workers from which it appeared that beta-naphthylamine and benzidine are both causes of tumours.

Dr. ACHILLES MÜLLER (Switzerland) summarised an experience of some thirty years in this disease, and indicated that the modern approach to manufacture, combined with routine cystoscopic examination, has led to its being mastered. Dr. CORNELIO BELLESINI (Italy) detailed a process of manufacture of benzidine in which workers have not developed any tumours even after twenty years.

The position in regard to these tumours in Britain was described by Dr. M. W. GOLDBLATT, who asked for an equitable system of compensation for workers who develop them.

Diseases of the Lungs

In a session on diseases of the lungs other than pneumoconiosis, Dr. T. A. LLOYD DAVIES described his clinical and experimental investigations into manganese pneumonitis, and Dr. K. M. A. PERRY read a paper on bagassosis.

Prof. A. POLICARD (France) spoke on his animal experiments on the effect of beryllium in the lungs. He found that beryllium sodium fluoride dusts provoke early and violent pulmonary œdema, resulting in death of the animals within 24 hours. Beryllium oxide dusts, on the other hand, cause hyperplasia of the mesenchyma of the lung tissue. Three types of reaction are found, the first being histiocyte pneumonia, the second granulomatous nodules, often with giant-cell formation, and the third cellular thickening of the alveolar walls. The granulomatous nodules seen after a few weeks' exposure persist for several months. Metallic beryllium and beryl do not seem to affect the lungs of animals.

Dr. E. H. SCHIÖTZ (Sweden) described the metal fever produced by copper dust. He preferred the name of "metal fever" to "metal fume fever" because in his experience the condition is produced by dust and not by fume.

The monocytic infiltration induced in animals' lungs by the introduction of manganese dioxide and beryllium oxide suggests that pulmonary lesions in men exposed to these dusts may be due to the same basic processes, despite clinical differences. It seems, too, that bagassosis, farmer's lung, broken wind in horses, and perhaps byssinosis, have a similar ætiology, as allergic conditions manifested as an acute bronchiolitis.

Toxicology

Dr. A. U. JORDI (Switzerland) gave an account of psychic disorders in industrial poisoning and referred to what he called a psycho-organic syndrome common to industrial poisoning by lead, mercury, and many organic solvents. The main features, he said, are loss of memory for recent events, slackening of all mental processes, depression and narrowing of interest, nervous irritability, rapid changes of mood, and insomnia. In mercury poisoning, tremor is the most obvious symptom; it progresses after removal to safe work, whereas in poisoning by organic solvents the symptoms usually clear unless the exposure has been long and severe. The changes are best studied in carbon-disulphide poisoning. In the treatment of the psycho-organic syndrome vitamins B and C and also male hormone have proved helpful.

Dr. M. BARSOTTI and Dr. G. CROTTI (Italy) spoke of epileptic fits in workers handling T.4. powder (trimethylenetrinitroamine), and Dr. R. A. MCFARLAND, Dr. NIVEN, and Dr. HALPERIN (U.S.A.) outlined a method for estimating the effects of various substances which interfere with the oxidated mechanisms of the central nervous system. The method involves the measurement and correlation of changes in light sensitivity with various criteria through blood analyses.

Dr. M. GAULTIER (France) discussed the ocular disturbances in cases of poisoning with methyl bromide, and Dr. A. AHLMARK and Prof. S. FORSSMAN (Sweden) read a paper on the testing of cerebral function by means of anæsthetics.

Atmospheric Pollution

Prof. PHILIP DRINKER (U.S.A.), in a paper written with Dr. W. A. COOK, referred to the difficulties in determining the maximum allowable concentrations of atmospheric impurities. The determining process, he said, is an art rather than a science, and it would be a serious mistake to consider any of the methods as accurate. Only a few substances, like carbon monoxide, have such well-defined systemic effects that safe exposures can be laid down with a high degree of precision. Most others, like benzol and carbon tetrachloride, fit best into zones of toxicity. He set out six such zones for a number of representative substances, ranging from the least harmful (like acetone) at concentrations from 500 to 2500 p.p.m. to the extremely toxic, like radon gases, at concentrations below 0·1 p.p.m. He believed that this classification of contaminants should help in the understanding and control of industrial health risks.

Mr. N. STRAFFORD discussed the determination of toxic substances in the air; Mr. C. N. DAVIES reviewed the history of fibrous dust filters; Prof. J. TEISENGER and Dr. B. SOUČEK (Czechoslovakia) described inhalation experiments designed to determine the absorption and excretion of carbon disulphide; and Mr. H. H. WATSON dealt with the physical properties of industrial dusts.

Radiant Energy

Dr. HERMAN LISCO (U.S.A.), speaking on the potential hazards and pathological aspects of radioactive isotopes, said that more use of radiant energy will in future be made by private research laboratories, government agencies, and in industry arising out of the peace-time developments of atomic energy.

Dr. G. FAILLA (U.S.A.) pointed out that it is hard to establish accurate limits for permissible exposure to

Digitized by Google

ionising radiations; but a committee in the United States have made some which they considered to be on the safe side. For ordinary X rays and gamma rays the permissible limit for exposure of the whole body was 0·3 r. per week, measured in air; for exposure of the hands it was only 1 r. per week, and for exposure of the whole body once in a life-time it was 25 r. for persons 21–45 years of age and 50 r. for persons over 45. For ordinary beta rays the limits are equivalent to the above in terms of energy absorbed per gramme of tissue at the level of the reacting skin cells. For fast neutrons the limits of exposure are related to a biological effectiveness factor which is 10 when the measurements are made in terms of energy absorbed in tissue; for slow and thermal neutrons the biological effectiveness factor is 5.

Dr. P. C. KOLLER described the chromosome fragmentation and the disorganisation of cell division caused by ionising radiations from X rays, gamma rays, neutrons, and alpha particles. The changes in the cells often result in their death and cause lesions in tissues which are slow in repairing. Controlled therapeutic doses of radiation may be employed to destroy cancer tissues through the damage induced in the mechanism of cell-division responsible for malignant growth. The changes induced by ionising radiation are not necessarily lethal to the cell; it may be only the distribution of the chromosomes which is altered. Tissues derived from such cells will be abnormal in their genetic constitution. Ionising radiation may induce changes in the "gene." If these occur in genes borne by the chromosomes of the sperm or ovum they will be transmitted to successive generations and spread in the species. Experimental evidence tends to show that in all living organisms genetic or hereditary changes are induced by irradiation, and that man cannot be an exception. The magnitude of the effects depends on the dose of radiation; these effects are cumulative and can be mitigated only by rigorous protective measures. It is therefore not enough to confine such measures to the protection of individuals; the genetic well-being of future generations is a major issue which must be equally considered when protective measures are devised.

Mr. W. BINKS spoke about the part played by the National Physical Laboratory in safeguarding the health of workers exposed to radiations. The service offered included examination of dental films carried by all workers exposed in factories and laboratories to radio-active materials and X rays. Experts from the National Physical Laboratory go out and measure the actual radiations in the workplaces.

Dr. L. H. GRAY asked Dr. Failla what is the basis of estimating the permissible doses of radiation and what are the actual absorptions by human beings as opposed to animals in experiments. He thought that care should be taken that the limit is not put too low. He also asked whether skin cancer from radiations can arise without there being any previous burn of the skin. In reply, Dr. FAILLA instanced the case of a technician in whom blood changes began within two years of exposure to an estimated radiation of 1 r. per day. In his opinion a limit of 0·3 r. per week is not too low. Skin cancer can arise without previous burning of the skin.

Dr. ETHEL BROWNING asked about the effect of small doses of radiations. In her examinations of the blood of all luminisers in the country, whose exposure was found to be low, it appeared that there was a stimulating effect on the blood from small doses and that curious cells appeared in the blood picture which were of the nature of immature monocytes. This effect appeared to be transitory, for similar cells were not found in her follow-up examinations of luminisers who had left the industry. Prof. J. S. MITCHELL said that these abnormal cells are difficult to classify, and we should lay stress on changes in total cell-counts rather than on counts of abnormal cells. He pointed out that skin cancers due to radiation appear on the dorsal aspects of the hands rather than on the flexor surfaces where atrophic changes occur. The time, he thinks, has come when the biochemists should become interested in the effects of radiation.

Mr. K. L. GOODALL outlined the practical problems that arise in guarding workers in factories from the effects of radiation, and he mentioned the Luminising Regulations drawn up by the Factory Department.

Dr. J. J. NIXON (U.S.A.) regarded the blood-count as a frail reed on which to assay the chronic effects from radiations. So many things affect the normal blood-count. One should pay attention to the trends of the blood-counts and the trends of the blood pictures in groups rather than in individuals. Other methods of investigation need to be developed.

Dr. KATHARINE WILLIAMS thought it important to know the permissible limit of exposure in a life-time, particularly for workers engaged in screening in X-ray rooms; and Dr. W. C. COX (U.S.A.) described how in the U.S. Army records of all X-ray exposures are kept so that more accurate knowledge may be obtained on which to lay down limits of exposure.

Disabilities

13. PULMONARY TUBERCULOSIS

DURING my first hospital appointment as a student I had a routine Mantoux test, which was negative. Four months later I had a series of hæmoptyses lasting a week, and a bad X-ray film did not show distinctly the lesion that was subsequently found in a much more advanced state. Three negative sputum tests and a normal sedimentation-rate, together with a normal axillary temperature, convinced the senior physician that the blood came from my nose (not examined); and after a fortnight's holiday I returned to ward work. During the summer I continued with my athletics, representing my country, and in the autumn I started training for the rugger season, during which I was expected to get an international cap. However, the war began and I was put on night duty. My finances were not good, and I began to spend less on food so that I had more for Saturday nights after rugger.

Definite symptoms appeared eighteen months after I had gone to my hospital. I could not get "fit," my "wind" was not good, I had a pain in my left side, and I began to cough. There was quite a lot of purulent sputum, which I was assured came from my sinuses, so I had a submucous resection and antral puncture. Soon I noticed I was losing weight, had indigestion, and my temper was awful. I started nightmares and night-sweats, and my voice was husky all the time. The pain was now acute and did not respond to heat, so I saw a doctor who found signs of cavitation. When he screened me and said "There's a cavity as big as a golf-ball, with a fluid level" my first instinct was to escape—to join a ship, anything rather than face the facts. My medical student friends firmly made me stay in bed and arranged for my admission to my teaching hospital. The local tuberculosis officer called to see me and arranged for an X-ray examination of my friends. It was a great relief to learn that none of them had been infected.

In hospital I was kept on "absolute bed rest," which probably did more harm than good since I could not read for long, and when I did have visitors I got overtired and had a much higher temperature than usual. A lot of my time was spent in a trough of depression, thinking how I could prevent my friends at home hearing of my condition and how I could redeem myself for the awful

Digitized by Google

crime of getting tuberculosis. I imagined myself an outcast, and it was not until my girl friend continued to visit me, despite all I did to dissuade her, that I realised the end of the world had not come. Eventually an eminent chest physician saw me, and at last the question of a sanatorium and the cost of treatment was raised. This was all taken out of my hands by my father, but I can imagine what a strain it could be for a less fortunately placed patient.

In time I was transferred to a sanatorium with my own room, and here for the first time I saw that one could get better. It was not that the will to get better had been lacking, but somehow one had never been given the prospect of a completely cured existence. My neighbour was a young man of similar age who had had tuberculosis before and relapsed, but was now improving. He gave me a new conception of tuberculosis—how one could live with the disease and what the limitations were. During his previous stay in the sanatorium he had wasted his time, but he was determined that this should not happen again; nor happen to me. Accordingly he argued with me on subjects I had hardly thought of, and made me buy new books on art, music, biography, and poetry. He insisted on my having a wireless set, and when eventually I got a gramophone with a lot of classical records and began to give recitals I realised how much I owed to his good advice: make the most of your time and you will not notice your illness. Furthermore, this interest in things other than sport broadened my outlook. That was before the days of art-therapy and most male patients did nothing except read detective stories. Those who were ambulant organised various communal activities and brought round the "glossy" magazines. Too much interest in communal activities is a bad thing, for it encourages the patient to feel he is important in his own little circle and to forget he has to live "outside." The "glossies" were a death symbol, the negation of all desire to get well and leave.

I had a successful artificial pneumothorax, but because of basal adhesions it was reinforced by a phrenic avulsion. The need for this had been carefully explained to me, as had the mechanics of collapse therapy, and I was beginning to take an interest in my A.P. rather than myself. This attitude is to be regretted, for patients become unduly alarmed if fluid forms and no longer consider themselves as a whole. Since my larynx was involved I was put on silence, which was very difficult to observe, especially when friends came to see me. I began to look and feel much better and to gain weight—but not self-confidence, so when I saw my parents for the first time since my diagnosis I was acutely embarrassed and felt very guilty towards them. They had been X-rayed by the authority that was paying for my treatment. I was very upset when told my brother had some infection, but a film six months later showed it had cleared up.

Life in a sanatorium, as in a gaol, imposes unphysiological restrictions, with the result that male and female patients develop "friendships" that will seldom withstand the trials of the outside world. Sometimes there is an engagement; and occasionally nurses, often tuberculous themselves, marry patients. This is a poor solution to the problem. At one time I got so immersed in the sanatorium life that I came to hate the visits of my girl friend because she symbolised the outside world with all its excitements and demands, to which I dreaded having to return.

One evening after a refill I felt rather breathless and found I had a temperature of 102°F. By the time I had called the nurse I was in great pain, hardly able to breathe, and when the doctor came I was collapsed. He immediately treated my spontaneous pneumothorax, and the next few days I was most unhappy though heavily "doped." Then followed three months' bed rest with occasional aspirations; but still the fluid formed, and, although my sputum had been negative since the A.P. was begun, the fluid contained tubercle bacilli in quantity. Now began a period of uncertainty; would I need a "thora" for my empyema or not? The surgeon said "yes" but the physician maintained there was no need in view of my good general health; so it was decided to wait and see.

A day came when I was allowed out of the building for a walk. I set off at a cracking pace and within five minutes was completely exhausted. This taught me a sharp lesson and I determined to find out the limits of my exercise-tolerance. My resting pulse-rate was 70 and on mild exercise 100 per min. If it rose to 120 I was very short of breath, but if it was higher than that I simply could not move, however fast I tried to breathe. This was a useful way of deciding whether I should go on with my walk or sit down and wait for my pulse-rate to fall. Naturally I was able to do more as I became adjusted.

When I left the sanatorium I spent some of my time with a former patient and we both noticed how difficult it was to find anywhere to sit down and rest, and practically impossible to stretch out at full length. How many hotel lounges have I visited in search of a quiet place when my rest hour was due! When a patient has just left a sanatorium he gets tired very quickly with the rush of modern life; he develops a feeling of despair and wishes vehemently to be back in his own cubicle, with the old routine. At this period, unless he takes things quietly and is given a lot of encouragement, he may relapse because of his inadequate general adjustment.

Two and a half years after diagnosis I returned to work in the wards, and I soon qualified. I have since done four years of house jobs of every sort. I do not feel equal to general practice, because if I have to be up at night I get too tired to carry on.

My day is usually as follows: Get up at 7.30 A.M., eat a good breakfast and travel to my clinic, where I write letters till 10.30 A.M. and then see patients until 1.30 P.M. An hour and a half for lunch, and then, according to the day, I either see more patients or go to a teaching hospital for a ward round. I always rest, lying flat, from 5.30 to 6.45 P.M., usually reading a medical book, and in the evening, after getting supper ready for 7.30, I read or write until 11.

I can play three sets of tennis (doubles) or run for a bus. I enjoy swimming, cycling, and walking. If I do too much I get overtired, and, knowing the symptoms, take a grain of sodium phenobarbitone, which gives me a good night's sleep. When my rest hour is due and I am away from home I never hesitate to lie on the floor—the most restful place—even if I am in a strange household. Every winter I develop a cough with mucoid sputum which I have examined regularly. I carry a piece of toilet-paper in my pocket to spit into, and throw it on the fire after use.

I go every six months to the chest physician who has always seen me, taking my latest X-ray film and B.S.R. result (never more than 4 mm.). Sometimes if I catch a cold and have "tuberculophobia" I go to be reassured. What do I fear most? A positive sputum, an indication of reactivation; sometimes when depressed I imagine I am getting a bronchopleural fistula, infection of the other lung, and secondary infection of the empyema necessitating rib-resection, thoracoplasty, and ultimately amyloid disease.

Two years ago I married the girl who, despite all difficulties, visited me regularly from my diagnosis. We spent our honeymoon walking in Switzerland, often going up to 7000 feet and once to 11,000 on the funicular. That, I felt, was the supreme test of my fitness and rehabilitation.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

THE danger of not being accepted as medical students never troubled us in the bad old days. So long as we could produce evidence of average scholarship and a headmaster's testimonial we were reasonably certain of a place. My year did, however, spend an anxious and very uncomfortable Registration Day. We attended at the appointed time and soon the waiting-room was packed with would-be students. Slowly and at first in a reasonably orderly manner we passed one by one into the Dean's office. Then the rumour started—that only a limited number of students would be accepted, on a first-come first-served basis. Instantly there was chaos, and most of us packed into the corner of the room nearest to the Dean's door. We stayed like this for several hours, a sharp struggle for priority breaking out each time the door opened.

The danger of non-acceptance may have appeared very real to us at that time but it was a ridiculous and undignified performance. The female applicants and a handful of older men stood aloof from the mêlée, and, many years later, one of the latter told me how he had viewed the scene with near incredulity, wondering how on earth this pack of rowdy youths could possibly be transformed into responsible doctors in the short space of six years. As an observer within the group he could study us closely as awkwardness left us, poise and self-confidence grew, and tidiness of dress began to assume some importance in our lives. He found the transformation astonishing.

In the modern sense we were not selected at all; we were just a group of middle-class boys who were either clever enough to win scholarships or whose fathers were well enough off to send us through medical school. We were a pretty average bunch, probably representative of the usual intake at provincial universities. A few fell by the wayside and never qualified, but the proportion was not high and I have yet to hear of a contemporary of mine who can be regarded as a professional misfit. Perhaps we were better than average or perhaps (dare I whisper it?) the danger of wastage has been over-emphasised in an attempt to make the best of a situation which current overcrowding has forced on us.

* * *

The following reflections on the Health Act should be sung in a West Country dialect to the air of "Villikins and his Dinah."

When I were a boy I were not very smart,
So they takes me and learns me the doctorin' art.
A general practitioner is what I became
—Now I earns a good livelihood by signin' me name.

When volks comes to zee me because they veels wrong,
To wan o' these yur specialists I passes 'em along,
I writes 'em a sustifikit to say they'm diseased
And the patients and the Minister is vurry well pleased.

If yur boy bain't azackly, if 'e bain't vurry bright
You do what I tells 'ee and then you'll do right—
Jest send un and larn un thiccy doctorin' game
—An' 'e'll earn a good livelihood a-signin' 'is name.

* * *

Examinations are in the news again. Candidates criticise: Censors condemn. But I go on taking them. A few nights ago the American Ambassador and I sat down to take the written part of the Conjoint finals. Just the two of us. The invigilator provided him with a large quantity of paper and me with a pile of soup-plates. One cannot write rapidly or legibly on a soup-plate whichever way up it is and naturally the time expired before I had even completed one answer. Last night I faced two examiners (one an old enemy of mine) across the green baize. He handed me a specimen. "What is that?" he said. "It looks to me," I replied without hesitation, "like a piece of melon—or possibly," I added as an afterthought, "paw-paw." He remained impassive. "You could not be further from the truth," he said, and walked out of the room. His co-examiner stared at the ceiling like the Frog Footman and said nothing. Once more the precious minutes ticked remorselessly by.

Before the trick-cyclists murmur condescendingly, "Elementary, my dear fellow," let me say that I have no further examinations to take. Why then, should I dream thus? Sometimes my pen runs out of ink; often I am disturbed and cannot concentrate; always the bell goes before I have really started. A frightful thought strikes me. Perhaps the Minister is planning a compulsory examination for all State doctors. But then, aren't all the best soup-plates going for export?

* * *

Finding a one-eyed man lurking in the hospital corridor I asked his business. In a Yorkshire accent he inquired whether I was the "vile diseases doctor." Ruefully admitting that I might be so described I was shown a long-standing ulcer of the leg, one of a series of gummatous incidents which were part of the man's very existence. He told me that he had been covering the ulcer with cobbler's wax and strapping it over with insulating-tape. Rather superiorly I informed him that modern treatment would soon take care of it if he attended very regularly. As it proved, he developed skin sensitivity to iodides, his oral condition limited the bismuth, and his dermatitic skin made one hesitate with arsenic. Penicillin was a disappointment and after three months the ulcer was as punched-out as ever and he was put on mercury as a last resort. During this time he had countless hospital applications and not a few of his own little-known proprietary unguents which on occasion I even had copied in the dispensary.

At last one day the ulcer showed indisputable signs of healing. "I knew it would, doctor," he said, "provided we had patience. But if I had been living in Hull it would not have taken a quarter as long." The last bit was rather a damper but I had to ask why. It appeared that some years ago when suffering from similar trouble he had taken his watch to be repaired at a shop in the back streets of that Yorkshire city. While he was inside the man behind the counter asked about his leg, inspected it, and announced that he could cure it in a fortnight. He retired to the rear of the shop and returned with some ointment in a boot-polish tin. The claim proved no idle boast and my patient had carried the ointment about with him for years as insurance against future trouble. He had finally surrendered it to his sister to cure a burn which was proving resistant to the machinations of her panel doctor. "I should never have parted with it," he concluded as he rose to go.

* * *

I was rather saddened by your correspondent describing how he had extracted a tooth. Out here in a Newfoundland outport (in Newfoundland outport means anywhere outside St. John's and corresponds to the provinces in England) I am 200 miles from a dentist, so I extract anywhere up to a hundred and fifty teeth a month. The difference between a doctor and a nurse is that a doctor is expected to be capable of doing a mandibular block. My patients order dentures from a mail-order firm in Chicago. They write away and are sent wax to take impressions themselves. Sometimes they come to me to do it for them. Sometimes the teeth fit, sometimes they don't. If they don't it's just too bad.

* * *

The misused idiom can also be amusing. M.O.: "Any serious illness?" Polish Fireman: "Noding sairioos—fifty-fifty ill sometimes." It seemed that "fifty-fifty" meant "slightly," for later, when I was testing his colour-perception, he called the paler shades fifty-fifty red, green, or what have you; he also volunteered the information that his auditory meatuses might be fifty-fifty dirty, as he had been working in the pits recently.

* * *

"SIR,—May I crave the hospitality of your columns to ventilate a point I was unable to thrash out owing to limited time at a recent meeting . . . ?"

Ventilation rather than castigation, by all means. But personally I prefer—if I have time—to nail my point to the mast and, with my back to the plough, steer my barque safely round Cape Metaphor and up the steep and thorny path until, at evenfall, I draw rein in the quiet reaches of Lunacy Verge Harbour.

Digitized by Google

Letters to the Editor

M.R.C.P. EXAMINATION

SIR,—The M.R.C.P. examination has often been subjected to criticism, not only by rejected candidates but also by the comitia of the Royal College of Physicians. The organisation of the whole examination will no doubt be carefully reviewed in the near future. Any views which I express here are personal and not official.

I was Senior Censor in 1942–43 when the entries were approaching 200. Although this is far short of the present hordes, the problems arising were similar.

Two questions which appear in the recent letters have been repeatedly discussed—viz., the requirement before entry of certain resident appointments or of a minimal interval after qualification, and the length of the clinical examination.

Before the late war, the requirement of resident appointments would probably have had little influence on the number of entries, since nearly all candidates could have complied with it. It might involve some difficulties with candidates from overseas, and possibly at the present time with those from the Services, but these could be overcome. There does not appear to be any valid permanent objection, and there are arguments in its favour, apart from any effect on the number of entries.

The length of the clinical examination has caused much anxiety. The arrangements for holding this examination, even at its present length, involve a serious burden on the hospitals to which the Censors are attached. This burden falls especially heavily on the registrars. The necessary preparations are now so time-consuming as to interfere definitely with their normal duties. Unless the entries can be materially reduced it would be difficult appreciably to increase the length of the clinical examination.

The question of reducing the number of entries by some fair method merits study for this and other reasons. The aim would be to discourage the weaker group and the candidate who "has a go at it."

The rapid elimination of candidates after entry also presents difficulties. No trivial test would be satisfactory. "M.R.C.P." suggests that 60% should be eliminated by "stiff papers." This method would introduce a competitive factor which has always been carefully avoided. Further, by throwing the emphasis on a written examination, it would defeat "M.R.C.P.'s" object of a more critical clinical examination. It would almost ask for freak questions, which are the worst possible criteria. Elimination by the clinical examination is more in accordance with the tradition of the membership.

It should be borne in mind that reading membership papers is very exhausting. For a qualifying examination 8 or 10 papers per hour can be assessed, and the strain is slight. Few examiners can mark more than 4 an hour for the membership.

The theme that success in the examination depends on luck runs through many of the letters. I do not believe that there is more luck in the membership than in other comparable examinations. It is frequently asserted that men who pass after many attempts, or even consistently fail, are as good as those who get through without difficulty. This statement is undoubtedly incorrect. The evidence is that the good man gets through and the weak man fails, though anybody may fail once. In view of the high percentage of rejections it is striking how many candidates pass at their first or second attempt, and it is these men who supply the great majority of the future leaders of the profession. Shortly after the first war I was told the names of the four men who had earned outstanding marks in the previous 4 or 5 years, and I have remembered them. All four now have international reputations.

Candidates here as elsewhere can be divided into three groups. The first group is above the borderline area, and can take a piece of bad luck and pass in spite of it. Indeed if bad luck is represented by an obscure neurological case, as seems to be almost universally accepted, the good man may profit by it.

The second group is below the borderline area, and rarely rises into it. Success of a member of this group may be attributed to a fluke rather than to ordinary luck.

The third group is in the borderline area, and wobbles exasperatingly above and below the pass line. It is the despair of the conscientious examiner. A viva-voce of 60 minutes and a clinical examination lasting all day would leave the examiner still in doubt, for this group is intellectually and permanently on the line. A piece of good luck may put up a man sufficiently to pass, but (as one letter-writer states) he is no better than when he was ploughed. A man from this group may certainly achieve success in after-life exceeding that of many of his contemporaries in the first group; but usually this is the result of personality and bedside manner rather than professional ability.

The pertinent question has been asked as to what is the significance of the examination. This has never been formulated and depends on tradition, for there are no rules limiting or directing the Censors.

The examination essentially demands a high standard, both theoretical and practical, in the basic principles of medicine. It may well happen that a candidate is not asked a single question or given a clinical case which he could not equally and fairly have encountered in a qualifying examination. And yet he may fail. An examiner in a final examination often gives a candidate a second chance. He will say "Think again, boy. Do you really mean that?" It is most unlikely that this will be heard in the membership. In the routine and method of examining a patient, and in the recognition and evaluation of obvious physical signs, the candidate must be right the first time.

It is here that many a candidate goes astray. Instead of studying over and over again one of the books on physical diagnosis, and making certain that in the wards the methods laid down are conscientiously followed until they become ingrained as an automatic routine, many assume that their knowledge and practice is already complete up to this stage, and that they are free to turn to more advanced branches of medicine. And so they fail repeatedly at simple cases, not because the examiner is pernickety but because they are unaware and remain unaware of their own shortcomings. The success of a fellow-student of no greater abilities but who has laid his foundations more surely only leaves them more than ever convinced that the examination depends on luck.

Thus the membership attests that a successful candidate has an assured knowledge of the general principles of medicine and is intellectually fitted to advance from this point by any one of many paths which he may select for himself, and it is on this basis that the membership has attained its present status.

London, W.1. HENRY TIDY.

HANDLING OF FOOD

SIR,—The deplorable methods of handling food, mentioned by Dr. Stanley Turner in his letter of Sept. 11, will be regretted by all. The problem is complicated by the variety of premises and the equipment which it is reasonable for them to instal for the special needs of their branch of catering.

I have yet to hear of any great effort to improve licensed premises in this respect. The minimum need is for the use of twin sinks for washing up, in order to permit the use of a detergent and for rinsing. In addition, the number of glasses should bear some relation to the expected peak rush of customers. False economy in the use of water charged by meter is an additional factor.

Elementary methods of food hygiene can only be taught in surroundings which are maintained at a suitable standard. We hope to initiate this here in the coming winter by remodelling of municipal catering premises, using existing materials as far as possible, so that when the pier restaurant and the like are let to catering contractors these can be demonstrated to hoteliers and their staffs and provide a standard for private catering establishments.

Catering staffs vary in their training, but all are looked down on. As long as a slightly shameful approach

Digitized by Google

is taken towards the preparation and serving of food and drink in this country just so long will it be difficult to influence staffs by propaganda. In Switzerland and other countries where this attitude does not exist there appears less cause for complaint.

W. S. PARKER
Cromer. Medical Officer of Health.

SIR,—In his letter of Sept. 11 Dr. Stanley Turner draws attention to the need for improvement in the *handling* of food if the spread of disease is to be avoided. May I suggest that there is also an urgent need for improved *inspection* of food in this country, and for closer collaboration between medical and veterinary authorities on this subject? I hope that means will be found to make available to your readers the paper which Mr. H. Thornton, chief veterinary officer of Newcastle-on-Tyne, submitted to the 66th Annual Congress of my Association. This paper, and the discussion which followed, provided ample evidence of how far we lag behind countries such as Denmark, the United States, and Germany, in matters of food-inspection, and of the danger to public health which results.

Points which arose during the discussion included: (1) absence of antemortem veterinary inspection of animals, especially "casualty cases," which so frequently harbour salmonella organisms; (2) the existence in some places of a knacker's yard alongside an abattoir; (3) the release to sausage-makers of meat only safe for use after sterilisation by heat; and (4) the sale at pet-food shops of uncooked meat, sometimes from tuberculous carcases, subsequently handled by the purchaser and occasionally even bought with a view to human consumption.

R. F. MONTGOMERIE
President, National Veterinary Medical
London, W.C.1. Association of Great Britain and Ireland.

SUPERNUMERARY NIPPLES

SIR,—May I draw attention to a condition which has been diagnosed as a supernumerary nipple by two experienced medical men? During hot weather about three years ago a male patient of mine, then aged 65, developed an ordinary yellow-headed pimple over his right breast. This was "squeezed" and a small amount of pus was evacuated. He subsequently developed a small keloid about the size of a pea at the site. I watched this from the beginning and there is no question about it. It is quite superficial, freely movable, has no deep attachments and no areola, and the skin over it is quite smooth with nothing suggesting the opening of any ducts. Before its appearance the skin was quite normal at the site of the keloid, which is not pigmented.

Brookwood, Surrey. H. M. STANLEY TURNER.

INTRAMEDULLARY NAILING OF FRACTURES

SIR,—My experience of the treatment of fractures by intramedullary nailing consists of only 3 cases, operated on in 1940, but it does explain my reluctance to use the method now. The idea of using a long trifin intramedullary nail for a fracture of the shaft of the femur occurred to me in 1939 after I had been using the Smith-Petersen trifin nail for fractures of the neck of the femur. After all, it is really only an extension of Smith-Petersen's original method of fixation. Messrs. Down Bros. made the nails for me; they were 15 inches long, trifin in cross-section, and of stainless steel. The cases in which they were used were transverse or short oblique fractures of the middle third of the shaft of the femur.

The main details and difficulties encountered were as follows. The fracture was reduced, using an orthopædic traction table, and a lateral incision was made above the greater trochanter, so as to expose the superior aspect of that structure, from which a circular piece of bone was removed to give access to the medulla. The trifin nail was introduced as far as the fracture line under X-ray control and then the difficulties started. It was essential not only to make sure of an almost perfect reduction in both planes but also to ensure that the fragments remained reduced while the nail was tapped across the line of fracture. The screening this necessitated was very considerable and dangerous to the operator if repeated at all frequently. The alternative of repeated films in two places was also very tedious and time-consuming. I did not attempt an open reduction of the fracture because this was the very procedure I was trying to avoid.

I understand that in the case of a fracture of the femoral shaft an open reduction is now usually employed; but if this is so, it is much simpler to plate the fracture. If plates with slots instead of round holes (Egger's type) are used, subsequent impaction is not prevented and all the advantages of intramedullary nailing are obtained through a single incision.

Norwich. G. K. MCKEE.

BINOCULAR MICROSCOPES

SIR,—I should like to thank Professor Hartridge for his letter of Sept. 11 in answer to mine of Aug. 14. He confirms that the real basis of eyestrain is interference with the normal muscle balance, and that this covers the imbalance of which I complain in converging-tube instruments, which compel convergence in spite of the fact that one's accommodation is relaxed. I notice, however, that he is scrupulously non-committal as to whether the microscopist does work with relaxed accommodation. I am satisfied that he does though the object always appears to be about ten inches away (presumably as a result of the association of ideas). An observation that seems to prove this is that, if you use a low-power ocular to examine objects with which you are familiar, they look much farther away than with your usual ocular. It is easy to see, therefore, why many people have jumped to the conclusion that they are accommodating. When working with a monocular instrument the unoccupied eye will be found to be focusing far beyond ten inches.

That the eyestrain produced by my converging-tube instrument is not produced by vertical displacement is readily verified by the method I always use for testing binocular instruments. The instrument is focused with one eye closed, and then the closed eye (which need not be the master eye) is rapidly winked. This does not give the normal muscle correction time to operate, and the displacement of the images is clearly apparent. I have a pair of binoculars in which this vertical displacement defies all my efforts to correct it, and I can entirely confirm Professor Hartridge's observations about the resulting eyestrain.

London, W.1. J. W. SHACKLE.

SPONTANEOUS RUPTURE OF THE RECTUM

SIR,—Mr. C. P. Allen's report (Sept. 4) prompts me to record a very similar case seen in this unit.

On the afternoon of Nov. 27, 1946, a man aged 47, who was manipulating a heavy brake lever in a shunting yard, felt a sudden pain in the rectum and lower abdomen. He had a desire to defæcate, but was unable to do so. Next day he passed a normal motion, but the abdominal pain grew worse, and on Nov. 29 he was admitted to hospital.

He was now in great pain and was dyspnœic. Temperature 98°, pulse 100, poor volume. The abdomen exhibited poor respiratory movements, board-like rigidity, and absence of peristaltic sounds. Rectal examination revealed tenderness high up but no other abnormal finding. Laparotomy was carried out and turbid fluid escaped. The pelvic colon was found to be adherent about a large collection of solid fæces lying free in the peritoneal cavity. An oblique rent 2 in. long was found in the anterior wall at the pelvirectal junction. The descending colon was loaded with fæces. The rent was closed, the abdomen closed without drainage, and a left inguinal colostomy carried out. The patient made a good recovery; the colostomy was closed on May 7, 1947, and he is now fit and well.

The striking features of our case are the length of time between the rupture of the rectum and the patient's admission to hospital, and the fact that the peritoneal cavity had made an almost successful attempt to seal off the escaping fæces; no fæcal odour was noticed until the adherent loops of bowel were gently separated. As Mr. Allen says, the condition may not be as rare as has been supposed.

ARNOLD S. ALDIS
Welsh National School of Medicine, Cardiff. Senior Assistant in the Surgical Unit.

Digitized by Google

BLOOD FOR TRANSFUSION

SIR,—The paper by Dr. Piney in your issue of Sept. 4 appeared to indicate dissatisfaction with the service provided by the National Blood Transfusion Service.

One of us (K. S. T.) when working at Colchester made many calls on this service, and Mr. Blaxhill was most helpful, providing on a number of occasions from 10 to 27 pints for any one patient. More recently we have treated a case of acute leukæmia here by exsanguino-transfusion, and Dr. W. Weiner, the regional transfusion officer, provided us with 36 pints of specially matched blood.

Not only are we satisfied with the supply of blood, but we would express the opinion that the serological work of the regional transfusion officer is of a much higher standard than can be expected of all but a very few pathologists.

W. P. U. JACKSON
Birmingham. K. S. THOMPSON.

SIR,—It will, I think, be generally agreed that even in the larger hospitals a temporary shortage of blood occurs from time to time, and that in many smaller ones the shortage is ever present. Discretion is therefore necessary in the use of blood for transfusion so that waste may be avoided.

Dr. Maycock defends the transfusion centres whose average good service needs no defence, and in arguing the defence, explains some of the shortage by accepting its existence.

It is true that there may be a relative deficiency of the rarer AB and B donors, and an even greater deficiency of AB and B donors who are also Rh-negative; but the rarity of AB and B donors parallels the rarity of the AB and B patients, and therefore an adequate donor service should prevent a deficiency.

It is over the methods required to provide such a service that I disagree with Dr. Piney. The provision of chits to enable donors to purchase extra rations would cease to be effective if and when rationing ends, and would then have to be replaced by a cash equivalent; moreover the reward would have to be disproportionately high in order to tempt a large enough number of people; for, as a race, we seem to react only to critical danger or great personal reward. It is for the same reason that I think good publicity can be only the adjuvant in the remedial mixture.

In my experience a solution may be found with junior house-officers in coöperation with the pathology department. If it becomes the regular practice for the house-man to interview relatives of patients who require transfusion, and explain in simple terms the maintenance of the hospital blood "bank account" and the necessity for special tests on the blood, it will be found that in most cases the relatives are willing to have their names placed on the donor panel to replace the blood when called upon to do so, and that the majority of these do in fact attend when asked. Moreover, after attending once they are usually willing to come again, and blood may thus be replaced in the ratio of 3 : 1 or more. The nucleus of a panel thus formed can be added to by volunteers, hypertensives, and others as opportunity offers.

This is, I feel sure, the key to the situation. Once such a practice had become commonplace, the replacement by relatives of blood transfused to patients would become an accepted routine, and the difficult problem of rewards, financial or other, need never arise.

The organisation of the collection and testing of blood must, for obvious reasons, be subject to local conditions: wherever possible the facilities of the regional transfusion centres should be used, but until these are sufficient it is possible to organise "local" transfusion services in conjunction with the pathology departments. Their success depends upon the active interest of all the staff, irrespective of seniority, and upon attention to detail in the matters of tact, courtesy, cups of tea, letters of thanks, and so on, all of which give rich dividends on the time invested.

Apathy is fatal, and especially to be avoided is such an apathetic manœuvre as the conferment on a junior resident of the placebo title of "transfusion officer," with duties so nebulous that they cannot be enforced, or the adoption of the complacent attitude that one man alone and without the wholehearted aid of his colleagues, can maintain a donor service.

R. D. POPHAM
Group Laboratory, Mile End Hospital, London, E.1. Assistant Pathologist.

INTERNATIONAL CONGRESS ON POPULATION

SIR,—Some mistakes seem to have crept into your report of Sept. 4 on the Cheltenham congress on population. The German birth-rate in 1933 was not (as Dr. Durand-Wever is supposed to have said), 8·7 per 1000, but 14·7. "At the height of the Hitler propaganda" (1939) it rose to 20·3, not to 14·9. The death-rate in Germany was not 5·8 per 1000 in 1938 but 11·6. No country in the world knows of such a low death-rate as 5·8. The Czechoslovak speaker can scarcely have said that there has been a "steady increase in the birth-rate of his country since the 1914–18 war," for quite the opposite happens to be the fact. In accordance with the general European trend, the Czechoslovak birth-rate declined steadily between 1920 and 1938, from 26·7 to 16·8. That the practice of contraception "has never found much support" in that country is not borne out by the facts. Every government aims at the "reduction of illegal abortions," but I have never heard of any special measure taken by the Czechoslovak government in this direction.

JOSEPHINE BRUEGEL.
Plaistow Fever Hospital, London, E.13.

*** We are obliged to Dr. Bruegel for drawing attention to these discrepancies. Nevertheless the figures we attributed to Dr. Durand-Wever tally with those of the official report, and we hope to be able to confirm that the Czechoslovakian delegate made the statements ascribed to him.—ED. L.

THE EOSINOPHIL CELL

SIR,—I was interested in Dr. Duran-Jorda's article of Sept. 18. During studies of the eosinophil cell, both stained and in its live state, extending over ten years, I have observed various activities which may be of interest in connexion with his theory of the origin of red blood-corpuscles, though they do not support his theory.

(1) The human eosinophil may contain spherical granules, or it may contain cubical or even oblong box-like granules. I have not seen ovoid granules, but they are by no means always spherical.

(2) Both eosinophils and neutrophils in certain phases of activity produce vesicles on their surfaces which tend to become separated from the cell and float away free in the surrounding medium. These vesicles vary in size from 1 μ to about 7 μ and often consist of cytoplasmic material without granules. Such vesicles or corpuscles may be very abundant in pathological material such as sputum or thin pus and are quite common in urine. Those produced by the neutrophil are very difficult to see under the microscope in the unstained preparation, but those produced by the eosinophil are more readily visible owing to their higher refringence and may very readily be mistaken for a red blood-corpuscle when their size is comparable.

(3) Often before becoming detached from the parent neutrophil or eosinophil such vesicles or corpuscles will receive a certain number of granules, and such granule-containing vesicles are often encountered floating loose from the parent cell. This type of vesicle has been observed to perform phagocytosis, although it contains no nucleus. The size of the vesicle bears no relation to its granular content, quite small vesicles often abounding in granules.

(4) Both the eosinophil and the neutrophil cell readily extrude long filopodia with which they perform prodigies of phagocytosis and which can be seen enwrapping shed epithelial cells in pathological fluids. At no time have I seen them perform phagocytosis of red blood-corpuscles in such material.

(5) It is clear from the above remarks that the free-floating corpuscles are not derived from granules, so that they would not qualify for erythropoiesis by the method suggested by Dr. Duran-Jorda.

(6) When the eosinophil cell is indulging in filopodial activity it may extrude the granules in the filopodium to a distance of over 100 μ from the nucleus. In the stained

Digitized by Google

preparation often only the granules and the nucleus are visible. In such a cell, although the granules are still within the cytoplasmic boundary the stained appearances suggest that they have lost all contact with the cell. Such a cell is often intensely active and may some minutes later be again rounded up into its classical shape.

The above activities of neutrophils and eosinophils were described and illustrated along with certain others in my paper[1] five years ago.

R. E. HOPE SIMPSON.

Epidemiological Research Unit, Cirencester.

BRITISH COUNCIL FILMS

SIR,—In your annotation on Films for Doctors (Aug. 28, p. 335) you say that "the British Council are finishing, for use overseas, films on artificial pneumothorax and on bronchography." To avoid any misapprehension may I point out that, although British Council medical films are made primarily for use overseas, they are also available for showing to professional audiences in this country. Those not held in the Central Film Library may be obtained from the Films Department, The British Council, 3, Hanover Street, W.1.

With regard to the films mentioned, "The Technique of Artificial Pneumothorax" has been in distribution for some time. "Bronchography" is still in production, and the council also has in production a series of films on plastic surgery.

PAUL REED
London, W.1. Information Officer.

DIETARY FAT

SIR,—Your leading article of Sept. 18 suggests four reasons for the craving for fat. The craving is not limited to fat alone but applies equally to the essential foodstuffs. Hoelzel, who frequently submitted himself to prolonged fasting to observe the effects of starvation, stated in a letter to A. J. Carlson[2] that "hunger appears to be a complex phenomenon which probably can be separated into hunger for proteins and carbohydrates, &c., as it does not seem as though satiety can be produced until all the elements of hunger indicated at any time are satisfied by the amount and kind of food craved."

Only a small amount of fat appears to be required, sufficient to add to the palatability of food; large quantities produce nausea and vomiting which do not occur with a surfeit of either protein or carbohydrate. The main indication for its use appears to be the advantages derived from its high boiling-point in cooking.

London, W.1. J.-JACQUES SPIRA.

THE PARKINSONIAN SMILE

SIR,—A peripatetic correspondent of Sept. 11 aptly compares the smile of Parkinson's disease to "the sun breaking through thunder clouds." The "smile" must be seen for the simile to be fully appreciated. It is rare in the idiopathic Parkinsonian, who is usually at a time of life when risibility is not easily aroused, but in those unfortunate younger persons suffering from the after-effects of epidemic encephalitis it is more easy to produce a "smile," and once seen it cannot be forgotten. On the other hand, your correspondent is not quite so happy in suggesting that Parkinson "patented the mask." As a matter of fact James Parkinson, in his original *Essay on the Shaking Palsy* (1817) made no reference, whatsoever, to the "facies" in his cases. Indeed, its characteristic appearance was not recorded till 1861, when Oppolzer of Vienna wrote: "Der Gesichtsausdruck ist ganz apathetisch." This was quoted and amplified later by Charcot and Vulpian. The term "facial mask" in connexion with paralysis agitans appears first in Pepper's *System of Medicine* (1880), whilst the term "Parkinson's mask" is first found in print in the original edition of Osler's *Textbook of Medicine* (1892) which refers to "the so-called Parkinson's mask." Fuller details on this small point may be found in my Note on the So-called Parkinson's Mask (*Brit. med. J.* 1923, ii, 25).

Sheffield. ARTHUR J. HALL.

1. *Brit. J. exp. Path.* 1943, **24**, 218.
2. *Amer. J. Physiol.* 1917–18, **45**, 120.

ŒSTROGEN AND BLOOD-SUGAR

SIR,—It may be of interest to other workers if I place on record my observation that patients treated with diethylstilbœstrol in oral doses of 5 mg. daily for 2–3 weeks have developed symptoms of hypoglycæmia.

Jerusalem. GEORGE BIRO.

MEDICAL RECORDS

SIR,—There is one difficulty on which "Medical Superintendent" in his interesting letter (Sept. 4) did not touch: given a secretary with the necessary qualifications and a physician or surgeon who requires her services, how do they find each other? I have been disengaged for some months and have not yet heard of a medical post I should like. There are numerous secretarial posts, but I have a predilection, regarded by my friends as slightly pathological, for medical work. One can, of course, advertise in the local press, or one could look up one's former employers or acquaintances influential in medical rectangles. The first method is slow and unproductive; the second doesn't appeal to me. Surely there is room for some sort of organised liaison between doctors and secretaries?

EUCILIUS.

PRIMARY TUBERCULOSIS WITH MENINGISM

Professor Choremis informs us that in both of the cases reported in his paper of Sept. 11 (p. 408) the children are in good health, with no signs of relapse or of development of disease, 9 months and 6 months respectively after the onset of their illness. Since his paper was written routine examination of the cerebrospinal fluid in similar cases has revealed three more children showing tubercle bacilli in the fluid on culture without any symptoms of meningitis.

Public Health

Deadly Nightshade Poisoning

IN addition to the five cases of belladonna poisoning reported from Portsmouth in our issue of Sept. 11 (p. 438), two further cases have since been treated at the Royal West Sussex Hospital, Chichester. Dr. G. T. Rutherfoord reports that at 11 P.M. on Sept. 7 two sisters, aged 5 and $3^1/_2$ years, were admitted to the hospital under the care of Dr. H. Seaward Morley with the diagnosis of acute belladonna poisoning. Between 2 and 2.30 P.M. on that day the children had been playing on a bombed site where they had eaten berries. At about 4.30 P.M. they had asked for buns, but were unable to eat them owing to dryness of the mouth. They refused a drink of water and were noticed to be hoarse. They were put to bed and slept from 5 to 7 P.M. when the younger child awoke and behaved strangely, and later brought up some brown vomit. Medical advice was sought, and she, together with her elder sister who also appeared unwell, were sent to hospital, the younger again vomiting before arrival.

On admission to hospital the younger child was fully conscious, though strange in her manner; her mouth was dry. The elder was semiconscious, and her mouth was not obviously dry. Apart from these points the physical signs in each were similar: the pupils were widely dilated and there were rapidly recurring jerky movements of the limbs. Gastric lavage was performed immediately. The washings were brown, and contained partly digested food, the only recognisable constituent of which was a quantity of plum skins, which had been taken at the midday meal. After the lavage a saline aperient was given.

During the first 12 hours after admission the children were very restless in spite of sedation. Thirst was conspicuously absent. Between 12 and 24 hours after admission they were delirious with hallucinations. After 24 hours there was gradual improvement until the 3rd day, when both children appeared perfectly well and happy, though their pupils were still widely dilated. A moderate degree of tachycardia (120–130 per min.) and pyrexia (99–100°F), which had persisted since admission, had by then disappeared.

Digitized by Google

It was impossible to be certain how many berries had been eaten, but the elder child stated that both she and her sister had taken one berry each. A plant taken from the place where the children had been playing was found to be *Atropa belladonna* (deadly nightshade).

Typhoid Fever on Clydeside

In the outbreak of typhoid fever in the Greenock, Port Glasgow, and Gourock areas of Clydeside, referred to on p. 471 last week, further investigation in Kilcreggan among people living beside the stream has revealed the presence of a carrier. This person, aged 80, had had typhoid fever at the age of 27 and had remained well since then. More accurate typing of the organism isolated from the numerous cases and from the carrier has shown that the type (F2) is an unusual one. One more case has occurred in Gourock associated with this stream; this is in a girl of 6 years who appears to have been ill at home for some time before the family doctor was called. One or two cases in this household are also under observation, and from the dates of sickening these are more likely to have arisen from the girl than from primary infection at the stream, though they too had taken part in picnics and had drunk water from the stream.

Parliament

A Short Session

A SPECIAL session of Parliament was opened by the King on Sept. 14 to pass for the second time through the House of Commons, before it goes once more to the House of Lords, the Parliament Bill which proposes to limit the power of the Lords to hold up legislation to a period of one year. As this measure is the only legislative business of the session the King's Speech was unusually short—74 words—but occasion was taken in the House of Commons in the debate on the Address to discuss matters of national and international interest.

Defence Measures

Mr. HERBERT MORRISON, Lord President of the Council, in his speech, for instance, made an important announcement on defence. All National Service men, he stated, due for release in the next few months who had not left their units by Sept. 14 must be retained for three months beyond the date on which they would normally have been released. In this way alone could the loss of trained men be halted. Releases in class B and on compassionate grounds would not be affected. This change would increase the strength of the Armed Forces by about 80,000. Mr. Morrison emphasised that the increase was in trained men who constituted the real need.

Mr. Morrison also assured the House that considerable progress had already been made with plans for assisting the population, for the reorganisation of the civil-defence services, and for the preparation of any legislation that might be necessary. While the measures which the Government were taking would have some effect upon our economy, it was hoped they would not jeopardise our recovery.

The Farm and the Factory

In the House of Lords on Sept. 16 Earl DE LA WARR moved:

That this House is of opinion that plentiful food imports are not likely to be available in the foreseeable future, and that it is desirable that the emphasis of our Empire and national economic policy and the allocation of capital resources and man-power should be adjusted to meet this change in our circumstances.

So long as economists advised governments, he continued, that in the reasonably near future there was still a possibility of our being able to return to the good old days of dear exports in exchange for cheap imports of food and raw materials it was unlikely that any government would tackle the problem of making the most of our own soil and our own Empire. The Emergency Food Council's estimate that world production of grain would equal pre-war supplies assumed good harvests, and as 60% now came from America and Canada, Lord De La Warr pointed out, we were therefore dependent on good weather in that hemisphere. Again, before the war 6 million tons of fats and oils were available for export: this year it was hoped to reach 4 million tons. Rice exports in 1948 were expected to be 40% above those of 1947, but, even so, they would be only 40% of the pre-war figure. The Emergency Food Council's figures also showed a reduction of 10–15% in the production of meat.

Lord De La Warr was further disquieted to see the great food producing countries increasing industrialisation at the expense of agriculture. Their populations were increasing, and they were tending to keep more food for themselves, and also making it more difficult for us to sell our exports. Where were our economists looking when they warned us against the danger of allocating too many of our resources to the development of our own soil? He recognised that to implement his motion would mean refocusing our national economic objectives, but it was, he held, a national approach to a national problem fundamental to our very existence.

The Earl of HUNTINGDON, joint parliamentary secretary to the Ministry of Agriculture, did not doubt the danger of the situation, but he urged their Lordships to take a balanced view. We were not likely to produce anything like all the food we needed in these islands and the problem therefore arose as to how we were to pay for our food imports. If we were going to have something to smoke and a reasonable cut from the Sunday joint we could only get them by our own efforts and ingenuity. He could see no good reason why this nation should not produce an abundance of the services and other things needed to pay for our imports. A more difficult question was whether other countries could pay for our foods in sufficient volume to enable us to buy in return. Population was undoubtedly increasing, but so, he added, was the scope for improvement of agricultural production. The Government recognised that food was the main and first essential and from the start they had devoted much of their energies to encouraging increased production in this country, in the Commonwealth, the Colonies and elsewhere overseas.

Viscount BRUCE of MELBOURNE thought that for some years we must act on the basis of sheer necessity for food, quite apart from any question of balance of payments, external payments or anything else. Britain would have to achieve and remain on a much higher level of agricultural production than formerly.

Lord BEVERIDGE suggested that making the best of a bad job had become one of our major industries, and that the debate fell within the scope of that industry. He believed that the long-term trend which throughout the 19th century had made our position better and better through our exchanging industrial products had been reversed and would continue to be reversed. But we must recognise the price of turning this country over more and more to agriculture from industry. There was a shortage of man-power, and if we had to grow a great deal of food ourselves we should have fewer houses and other things we need. We must therefore take care not to develop agriculture unless it meant that we could get our food by home production more cheaply in terms of labour than we could get it by exchange from abroad. Agriculture must prevail on its own merits, because we needed it, and not by protection. He agreed, however, that we were bound to make agriculture both more productive per man and more attractive of men in relation to industry than it was at present. He also stressed that people should be made to realise that our relatively easy prosperity had gone for ever.

Ending the debate Viscount ADDISON, Lord Privy Seal, said that according to our present programme, which seemed likely to be attainable, we aimed at a tonnage of bread grains of 2,750,000 tons, and a potato yield of 7,250,000 tons. It was obvious, he said, that more food must be produced in the sterling area and long-term contracts, leading it was hoped to increased production, had already been made with colonial countries for wheat and flour, dairy products, meat and bacon, eggs, vegetable oils, sugar, dried fruits, and coffee.

It was true that there was a world scarcity, though there might be here and there a successful harvest. Vast

Digitized by Google

numbers of the increased millions of the world were underfed. Before the war there were millions of people in this country underfed, and now, badly off as we were, a good many were better fed than before, especially the children. The Government would like a lot more to be better fed. He protested against the suggestion that the increase of production from our land meant a diversion from our manufacturing efforts, but the Government were quite ready to accept Lord De La Warr's motion.

Obituary

EUGÉNIE LEESON WILLIS

M.A., M.B. CAMB., F.R.C.S.

Miss Willis, who died on Sept. 12, at the age of 38, received her medical education at Cambridge and at the Royal Free Hospital, qualifying for the Conjoint diploma in 1935, and obtaining the Cambridge M.B. two years later.

After serving as a house-surgeon at her own medical school, and holding other resident appointments in the South of England, she took the English F.R.C.S. in 1939, and shortly afterwards came to the North as resident surgical officer at the Oldham Royal Infirmary. From 1942 she specialised in orthopædic surgery, and during her short career she did valuable work, mainly at the Manchester Royal Infirmary. As chief assistant to the orthopædic department there from 1942 to 1945, when the staff was severely depleted by the calls of the Services, she had to bear a heavy burden in the routine care of hundreds of battle casualties. When the fighting ceased she was able to turn her attention to a wider sphere of work as visiting orthopædic surgeon to the municipal hospitals of the county borough of Oldham, and as orthopædic registrar to the Manchester Babies Hospital. She also served the Manchester University as a teacher in the departments of anatomy and orthopædic surgery.

Yevonde, Manchester

But what promised to be a busy and active career was gravely threatened in its earliest days by the development of the chronic disease from which she died. Her courage in facing her disability, and her determination to work despite her grave affliction, earned the admiration and respect of her many friends, to whom her memory will always be vivid. D. LL. G.

Births, Marriages, and Deaths

BIRTHS

BARKWORTH.—On Sept. 13, in London, the wife of Dr. F. B. S. Barkworth—a son.

HUNT.—On Sept. 15, in London, the wife of Dr. W. E. Hunt—a son.

JEAVONS.—On Sept. 14, to Dr. Mary Patricia Jeavons (née Woodhouse), wife of Flight-Lieutenant P. M. Jeavons, M.B.—a son.

PEARCE.—On Sept. 15, in London, the wife of Dr. Richard Pearce—a daughter.

SAUNDERSON.—On Sept. 16, in London, Dr. Elizabeth Flett, wife of Mr. William Edward Saunderson—a daughter.

WHITNEY.—On Sept. 9, at Broseley, Shropshire, to Dr. Freda Whitney (née Bannister), wife of Dr. Rupert Whitney—a son.

MARRIAGES

JONES—MORRIS.—On Sept. 16, at Llansannan, Henry Russell Jones, M.R.C.S., to Joan Denman Morris.

DEATHS

DANIEL.—On Sept. 18, at Petersham, Surrey, Alfred Wilson Daniel, M.D. Camb.

HENRY.—On Sept. 17, John Rea Henry, M.B. Belf., aged 64.

HINGE.—On Sept. 15, at Woburn Sands, Henry Alexander Hinge, C.B., C.M.G., D.S.O., M.R.C.S., major-general, R.A.M.C. retd, aged 79.

SLOME.—On Sept. 12, in London, Irving Somerset Slome, M.B. Lond., R.N. Cape Town.

STEWART.—On Sept. 16, at Sleights, Yorks, William Stewart, M.B. Edin.

Notes and News

NATIONAL HEALTH SERVICE

MR. BEVAN REVIEWS THE SITUATION

SPEAKING at the annual dinner of the Society of Medical Officers of Health, held in London on Sept. 16, Mr. ANEURIN BEVAN, Minister of Health, said that controversy over the National Health Service Act had been inevitable, but he now looked forward to a period of fruitful collaboration in one of the greatest enterprises ever undertaken by an administration in peace-time. The transition had so far gone with unexpected smoothness, thanks largely to the efficiency of the Civil Service. The object was to secure coöperation, for the benefit of the public and the advancement of medical science, between the State financial machine and the voluntary workers who (though foreigners could not believe it) administered the service. The national genius was to get hold of a principle of this sort "and warm it up by the enterprise of ordinary men and women." No doubt many defects would be revealed and call for improvising ability. He had been much afraid that the middle and professional classes (for whom illness was often especially harassing) might be persuaded to stay outside the service, by people who told them that it was for the needy. But the danger of "a schizophrenic service" had almost passed. The last figures showed that 92–93% of the population had already signed up, and new signatures were coming in at the rate of 150,000 a week. It looked as though nearly everybody would be included by the end of the year, and he was delighted at this because it meant that the N.H.S. would be a classless service. It had been fully expected that during the first year there would be a rush for many of the facilities provided. The natural desire to get something for nothing would wear off; but the new demand was also largely due to real needs which people previously could not afford to meet: it was surprising, for example, to find how many old-age pensioners had been buying their spectacles at Woolworth's. Dentists were now coming into the service more quickly, and no doubt as time went on most of them would be in the scheme.

Many had feared (Mr. Bevan continued) that the Act would produce a split between different parts of the service: and on the surface it had looked as though they were justified. But he had always believed that the medical officer of health would join up what would otherwise be disjointed; and in fact M.O.H.s had done magnificent work of this kind in the past year. He was very keen on health centres, and was anxious that some should be built quickly. "But we're trying to do an awful lot of things at once." If he had to choose between the preventive effects of a good new house and the curative effects of a new health centre he would choose the house: enough new houses would diminish the need for health centres. Important though the therapeutic contribution to health was, the silent contribution of preventive medicine was far greater—made through such things as a pure piped water-supply, building regulations, sanitary inspection, and the Acts governing food and drugs. He hoped that the M.O.H. would continue to serve as a unifying principle in the health service.

Dr. FREDERICK HALL, president of the society, was glad to think of the M.O.H. as a bridge between preventive and curative medicine: but some bridges were temporary, some were swept away, and some were preserved merely as ancient monuments. He hoped this particular one would be given strong support and firm foundations, part of the support being financial. The Act would be very difficult to operate unless all possible means were used to limit the incidence of disease—which was not being done at present. In replying to Dr. J. GREENWOOD WILSON's toast of The Guests, Dr. GUY DAIN, chairman of the council of the British Medical Association, said that the terms of service for different branches of the profession must be so integrated that no branch offered outstanding financial attractions. The association and (he was sure) all doctors would do their best to see that the service was a success, though they would point out defects as these occurred. The Minister had solidified the profession in a way never thought possible and he should make good use of its unity. The best results would come from the service if its members were well organised and well able to express their views. Sir WYNNE CEMLYN-JONES also responded.

Digitized by Google

SELECTION OF NURSES FOR A MENTAL HOSPITAL

THE Cassel Hospital for Functional Nervous Disorders has a respectable tradition in the training of psychiatric nurses, and indeed offers a hospital certificate in psychological nursing. As the annual report for 1946 points out, the nursing of patients with neurosis makes considerable demands on the emotional maturity of the nurse; and in the last few years nurses joining the staff have been chosen by a selection procedure which endeavours to assess this quality.

The system was introduced by Dr. C. H. Rogerson (who was later succeeded as medical director by Dr. T. F. Main). He and his medical and nursing colleagues agreed that the personalities of suitable candidates would differ widely and that the one question to be answered was "how is she likely to perform in this hospital?" In the attempt to answer it each candidate is asked to attend for a whole day —from 9.30 A.M. till tea-time—as one of a group of eight.

Facts about her age, schooling, training, and experience are collected on the application form, as well as details relating to psychosomatic symptoms and general health. When she arrives she is received by the matron and a sister in the staff common-room, and is introduced to her fellow candidates over a cup of tea. Toward 10 o'clock the matron tells the group something of the hospital and its purpose, and the sister then takes them on a tour of the premises, introducing them to any members of the staff they meet, and answering their questions. At 10.45 A.M. they return to the common-room and meet the rest of the staff over morning coffee. At 11 A.M. they go to another room, and sitting in a friendly semi-circle round the sister begin their written tests. These aim at giving the candidates opportunities "to respond, in their own characteristic ways, to the same evocative emotional stimuli," and thus to reveal something of their own emotional patterns. Candidates are therefore asked to give an account of the scene portrayed in a picture (Murray's cards are used), and to write a series of sentences each containing a stimulus word (15 seconds being allowed for the composition of each sentence). Each nurse is invited to write a short description of herself as a person; to describe in two minutes the most exciting moment of her life; and to do an intelligence test of the kind which shows capacity to learn.

This carries the group to lunch-time, when they lunch in the cafeteria with staff and patients. At 2 o'clock interviews begin. Two psychiatrists are available, each interviewing four candidates, the interviews lasting 10–40 minutes; meanwhile the matron sees each candidate, as soon as she is free, for a quarter of an hour. The sister conducts them to and from the interviews and gossips with them between whiles.

At the end of the interviews the psychiatrist has in his hands much relevant material about each candidate: the details on the application form, the intelligence quotient, the summary of "personality pointers," and the material he has elicited in talk. The atmosphere throughout the test is made so easy and informal, and the candidate's self-respect is so carefully regarded, that she is usually ready at the interview to tell more about herself, and even in some cases to discuss "stress points" within herself. The matron decides whether she likes her or not—an important decision, since she must work with her.

At 3.30 the whole group meet again with one of the psychiatrists, who initiates a group discussion; her each candidate is seen, so to speak, in social action, and shows her capacity to form easy reciprocal relations with others. At 4.30 the candidates take tea with the matron and are given the opportunity to talk over and criticise the selection procedure; this enables them to leave the hospital on a note of professional respect and equality. The selection team—psychiatrists, matron, and sister—then discuss them, and the matron, aided by the selectors, makes her final choices. The results have shown the value of the tests, and the method has proved acceptable to nurses, whether engaged or not.

Committee on Social Workers in Mental Health

The Minister of Health has set up a committee "to consider and make recommendations upon questions arising in regard to the supply and demand, training and qualifications of social workers in the mental health service. The committee is to present an interim report on these questions in relation to psychiatric social workers." The members are:

Prof. J. M. Mackintosh (chairman); Dr. J. B. S. Lewis, Dr. R. M. Bates, Dr. R. H. Parry, Mr. Bryn Roberts, Dr. Kenneth Soddy, Miss S. Clement Brown, Miss Eileen L. Younghusband, Miss C. V. Barclay, Miss J. M. Mackenzie. Mr. A. Forbes of the Ministry of Health will act as secretary.

Charing Cross Hospital

Field-Marshal Viscount Montgomery will deliver the inaugural address to the medical school on Thursday, Oct. 7, at 4 P.M.

Welsh National School of Medicine

On Tuesday, Oct. 5, Prof. E. D. Adrian, O.M., F.R.S., will deliver the opening address of the session at the school, 10, The Parade, Cardiff. He is to speak on the Aims of Medicine.

Society of Apothecaries

There has been an alteration in the programme of the course on modern therapeutics announced in our advertisement columns last week. Dr. Basil Parsons-Smith will now give the lecture on Oct. 25. He will speak on Hypertension.

Royal College of Obstetricians and Gynæcologists

Dr. Emil Novak, associate in gynæcology in the Johns Hopkins Medical School, Baltimore, will deliver the biennial Anglo-American lecture on Friday, Oct. 1, at 2.15 P.M., at 1, Wimpole Street, London, W.1 (and not at the college as previously announced). He is to speak on Certain Functioning Tumours of the Ovary.

Royal Society of Medicine

Dr. Philip S. Hench, of the Mayo Clinic, will give the Samuel Hyde lecture before the section of physical medicine of the society on Wednesday, Oct. 13, at 4.30 P.M. The title of his lecture is A Critical Evaluation of Current Remedies for Rheumatoid Arthritis. The officers of the section invite those who are not fellows of the society, but who wish to attend, to apply for tickets to Dr. Doris Baker, the hon. secretary of the section, at 1, Wimpole Street, London, W.1.

Institute for the Scientific Treatment of Delinquency

Dr. J. D. W. Pearce is giving a course of 12 lectures on the Psychology of Delinquency, on Thursdays, at 6.30 P.M., beginning on Sept. 30. Mr. Hermann Mannheim, DR. JUR., and Dr. Edward Glover will also give six lectures on Criminology and the Psychopathology of Crime, at 6.30 P.M. on Tuesdays, during November and January. Particulars of these and other lectures to be given at the institute may be had from the secretary, 8 Bourdon Street, Davies Street, London, W.1.

Commonwealth Travelling Professorship

The Royal College of Physicians has nominated Dr. G. W. Pickering, professor of medicine in the University of London at St. Mary's Hospital, as Commonwealth travelling professor for 1949. He will visit Australia and New Zealand in the early part of that year.

Mr. Arthur Sims, of New Zealand, endowed a Commonwealth travelling professorship, under the ægis of the Royal College of Surgeons of England, the Royal College of Physicians of London, the Royal Australasian College of Physicians, and the Royal Australasian College of Surgeons, providing for the appointment annually of a travelling professor to visit England, Australia, New Zealand, South Africa, and Canada to assist in the advancement of medical science either by lecturing, teaching, investigating, or engaging in research.

Sir Weldon Dalrymple-Champneys, F.R.C.P., will take office as chairman of the council of the Royal Sanitary Institute on Oct. 1.

CORRIGENDUM.—*Meningo-encephalitis in Man Due to the Louping-ill Virus.* On p. 454 the last line of the first column should read: ". . . total of 500,000 units. . . ." In the 9th line of the second column, for Dec. 2 read Oct. 2.

Diary of the Week

SEPT. 26 TO OCT. 2

Tuesday, 28th

EUGENICS SOCIETY

5.30 P.M. (Burlington House, Piccadilly, W.1.) Mr. Paul Bloomfield: The Eugenics of the Utopians—the Utopia of the Eugenists.

Wednesday, 29th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1

10 A.M. Mr. A. C. Deverell: Relationship of Dental Disease to Diseases of the Throat, Nose, and Ear.

Friday, 1st

ROYAL COLLEGE OF OBSTETRICIANS AND GYNÆCOLOGISTS

2.15 P.M. (1, Wimpole Street, W.1.) Dr. Emil Novak (Baltimore): Certain Functioning Tumours of the Ovary. (Anglo-American lecture.)

UNIVERSITY OF GLASGOW

3 P.M. (Chemistry building.) Prof. Geoffrey Jefferson, F.R.S.: Contribution of Sir William Macewen to Neurosurgery and its Sequels. (Macewen lecture.)

Digitized by Google

OCT. 2, 1948 PAGES 517 TO 554

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6527 LONDON: SATURDAY, OCTOBER 2, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Penicillin in Diphtheria..... 517

Thymine, Folic Acid, and Vitamin B_{12} in Nutritional Macrocytic Anæmia, Tropical Sprue, and Pernicious Anæmia
Prof. TOM D. SPIES, M.D.
R. E. STONE, M.D.
Prof. G. G. LOPEZ, M.D.
Prof. FERNANDO MILANES, M.D.
R. L. TOCA, M.D.
TOMAS ARAMBURU, M.D..... 519

Exchange Transfusion in Hæmolytic Disease of the Newborn
P. L. MOLLISON, M.R.C.P.
M. CUTBUSH, B.SC..... 522

Influence of Restraint on Automatic Movements
Prof. VLADIMIR VUJIC, M.D.
KOSTA KURTES, M.D..... 527

Primary Carcinoma of the Liver in a Boy Aged 15
A. E. BEYNON, M.R.C.S..... 528

Delayed Pneumonitis in a Beryllium Worker
J. N. AGATE, M.R.C.P..... 530

SPECIAL ARTICLES

Organisation of an Arthritis Clinic
A. A. MCINTOSH NICOL, F.R.C.P.
W. GRANT WAUGH, F.R.C.S.E.
IAN C. COWAN, M.B.
JOHN HARKNESS, M.B..... 541

Infertility: Family Planning Association's Conference..... 542

Pneumoconiosis 544

The New Zealand Health Service 545

Medical Defence Union..... 545

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents..... 546

LEADING ARTICLES

THE HOUSE COMMITTEE..... 535

BERYLLIUM GRANULOMATOSIS... 535

TREATMENT OF HÆMOLYTIC DISEASE OF THE NEWBORN.... 536

ANNOTATIONS

Research 537
Tuberculosis in India..... 538
Amœbæ in Britain..... 538
Tissue Heating by Microwaves (Radar) 538
Neurosurgical Service..... 539
War Researches on the Cornea... 539
Pterins for Leukæmia..... 540
The Laws and the Judges..... 540

PARLIAMENT

Army Cadets' Deaths from Heat-stroke..... 550
Adjournment 550
Question Time..... 550

LETTERS TO THE EDITOR

Accidental Intra-arterial Injection of Drugs (Dr. R. Wyburn-Mason)..... 547
Dietary Fat (Dr. Z. A. Leitner).. 547
Supernumerary Nipples (Dr. Gordon Hesling)..... 548
Polyarteritis Nodosa (Dr. A. I. Suchett-Kaye) 548
Polythene Tubing in Blood Transfusion (Dr. William Walker) 548
Spontaneous Rupture of the Rectum (Mr. Robin Burkitt, F.R.C.S.E.) 549
Letter to a Nephew..... 549
Private Patients not Admitted (Mr. Somerville Hastings, F.R.C.S., M.P.)..... 549
Selection of Teachers..... 549
The Cassel Hospital (Dr. T. F. Main) 549

REVIEWS OF BOOKS

Treatment of Heart Disease. Prof. W. A. Brams, M.D..... 533
Major Endocrine Disorders. S. L. Simpson, F.R.C.P..... 533
Surgical Treatment of the Abdomen. Prof. F. W. Bancroft, F.A.C.S., Prof. A. Wade, F.R.C.S..... 533
Nouvelles techniques de traitement des fractures. H. Godard, R. Michel-Bechet..... 534
Hodgkin's Disease and Allied Disorders. Henry Jackson, Jr., M.D., Prof. Frederic Parker, Jr., M.D..... 534

OBITUARY

William Frederic Harvey..... 550

NOTES AND NEWS

Physiotherapy Congress..... 553
Hospital Guide for Liverpool Region 553
Index for Film Records..... 553
Aseptic Dispensary..... 553
Smoke Abatement..... 553
Medical Care in Rural America.. 553

University of London..... 554
University of Leeds..... 554
Society of Chemical Industry.... 554
British Orthopædic Association.. 554
Demonstration of Contraceptive Technique 554
Royal Institute of Public Health and Hygiene..... 554
Institute of Neurology..... 554
West London Hospital..... 554
Association of Optical Practitioners 554
Exhibition of Medical Photography 554

Diary of the Week..... 552
Appointments..... 554
Births, Marriages, and Deaths... 552

ANAHÆMIN B.D.H.

The treatment of pernicious anæmia with Anahæmin B.D.H. is characterised by—

1 the small volume of effective doses

2 the infrequency of maintenance doses

3 comparative freedom from reactions

Each batch of Anahæmin B.D.H. is clinically tested before issue.

THE BRITISH DRUG HOUSES LTD. LONDON N.1

Digitized by Google

OXFORD MEDICAL PUBLICATIONS

JUST PUBLISHED

A NEW (FIFTH) EDITION OF

POST-MORTEM APPEARANCES

By JOAN M. ROSS, M.D., B.S., M.R.C.S., L.R.C.P.

Adviser in Pathology to the Ministry of Supply; late Reader in Pathology, University of London; Morbid Anatomist to the Royal Free Hospital; Assistant Pathologist to St. Mary's Hospital

Contents include: General Remarks—Death from Causes other than Disease—General Metabolic and Deficiency Diseases—General Infections—Diseases of the Digestive System—Diseases of the Kidney—Diseases of the Respiratory System—Diseases of the Ductless Glands—Diseases of the Blood and Blood-forming Organs—Diseases of the Cardio-vascular System—Diseases of the Nervous System—Still Births and Neonatal Deaths—Anatomical Normals (Averages)—Length and Weight of Fœtus—Approximate Weight of Organs of Newborn Child—Dates of Ossification of Principal Bones—Ages of Eruption of Teeth—Age of Fœtus—Changes in Umbilical Cord—Index.

318 *pages* 8*s.* 6*d. net*

OXFORD UNIVERSITY PRESS

ADVANCES IN PEDIATRICS

VOLUME III

Editorial Board

S. Z. LEVINE, Cornell University Medical College, New York.
A. M. BUTLER, Harvard Medical School, Boston.
L. E. HOLT, Jr., New York University, College of Medicine.
A. A. WEECH, University of Cincinnati, College of Medicine.

1948 6″ × 9″ 373 pages 77 illustrations 45s.

REMINGTON'S PRACTICE OF PHARMACY

Ninth Edition

By E. F. COOK, P.D., Ph.M., M.Sc. and E. W. MARTIN, Ph.C., B.Sc., M.Sc., with the collaboration of more than 40 Associate Editors.

This new edition of the well-known standard text book has been thoroughly revised and rewritten and contains up-to-date information on all branches of pharmacy and pharmaceutical chemistry, including biological products and processes, insecticides, cosmetics, business administration and surgical supplies.

Published by The Mack Publishing Company. *London Agents:* Interscience Publishers, Ltd

1948 8⅛″ × 11¼″
1550 pages, more than 800 illustrations 90s.

INTERSCIENCE PUBLISHERS, LTD.
2a Southampton Row London, W.C.1

ALLEN & UNWIN

Books by CHARLES BERG

Clinical Psychology

This brilliant and detailed review of the whole subject of clinical psychology concludes with a critical analysis of past treatment and revolutionary suggestions for the future. It is a case book of the neuroses and their treatment and cites examples from the simplest worries and anxieties, through increasing severity of stresses, to incipient major disorders. Straightforward, realistic and fascinating, the reader will hardly realise how much information he is assimilating. It is a book that every doctor can read and enjoy.

500 *pages.* 25s. net

Deep Analysis

The complete analysis of an individual case which throws considerable light upon the working of the human mind.

"There is no article or book we know of which puts on record quite so clearly how psychoanalytic interviews are conducted, and it can be warmly commended."—*The Practitioner.*

12s. 6d. net

40 MUSEUM STREET, LONDON, W.C.1

Digitized by Google

PENICILLIN IN DIPHTHERIA

REPORT OF A SUBCOMMITTEE OF THE PUBLIC HEALTH LABORATORY SERVICE*

IN this investigation the penicillin-sensitivity of 284 strains of *C. diphtheriæ* isolated in different parts of the country was measured. An attempt was also made to find out if penicillin treatment shortened the time of carriage of *C. diphtheriæ* in acute cases of faucial diphtheria and eliminated the organism in persistent throat carriers. Information on the clinical effect of penicillin in cases of diphtheria was not sought. Though there is general agreement that *C. diphtheriæ* is sensitive to penicillin in laboratory tests, the evidence for this view mainly rests on separate reports on a few strains (Long 1947). This criticism also applies to much of the work on the penicillin treatment of acute cases and chronic carriers, though Karelitz et al. (1947) have treated 80 acute cases of diphtheria with encouraging results. Because of the low incidence of diphtheria in this country we tried to secure sufficient material for examination by carrying out our tests in eight laboratory areas.†

TABLE I—PENICILLIN-SENSITIVITY TESTS CARRIED OUT IN SEVEN LABORATORIES ON 284 STRAINS OF *C. diphtheriæ*

Bacteriostatic level (unit per ml.)	All strains	Gravis	Intermedius	Mitis
1·0	2	2	—	—
0·6	32	14	6	12
0·3	65	34	15	16
0·2	125	40	27	58
0·1	38	4	12	22
0·06	14	1	2	11
0·03	8	—	—	8
Totals ..	284	95	62	127

SENSITIVITY OF STRAINS TO PENICILLIN

Technique.—A standardised and stabilised penicillin solution was distributed every fortnight by Dr. Joseph Ungar, of Glaxo Laboratories Ltd., and this was used for all tests. The requisite amount of penicillin was added in bulk to nutrient broth (pH 7·5) which contained 1% 'Lab Lemco,' 1% proteose peptone, 0·5% sodium chloride, and 5% of a single batch of heat-inactivated Seitz-filtered horse serum; 5 ml. of this broth was used for each dilution of penicillin, which ranged from 0·6 to 0·03 unit per ml. of medium. For each strain of *C. diphtheriæ*, therefore, six tubes containing penicillin were inoculated together with a broth tube without penicillin. In addition a similar control series of tubes inoculated with the Oxford staphylococcus accompanied each strain under test, and when a batch of strains was tested it was customary to put up controls inoculated with stock strains of the three types of *C. diphtheriæ*.

Each tube was inoculated with an arbitrary standard loopful ('Nichrome'-wire loop of internal diameter 4 mm.) of an overnight culture of the organism grown in the broth medium. Tubes were then incubated at 37°C for twenty-four hours. After thorough shaking the tubes were examined and the turbidity was recorded. From the tube at the visual end-point and from the tube containing the next highest concentration of penicillin a standard loopful was then spread on half a blood-agar plate. The number of colonies developing after overnight incubation was estimated and compared with the number obtained from a control tube. This control, with which it was intended to estimate the size of the original inoculum, was prepared by adding a standard loopful of an overnight broth-culture of the strain under test to 5 ml. of the broth medium, and plating out immediately. Subcultures from tubes yielding numbers of colonies greater than half the number from the control were, for the purposes of the test, considered not to show inhibition; the first tube from which subculture gave less than half the number of colonies from the control tube indicated the penicillin sensitivity of the strain.

Results.—Most of the strains were tested in each of two laboratories, and only very occasionally was there more than a one-tube difference in the sensitivities recorded. Such differences were observed with twelve strains, and these were retested before they were recorded. Under the conditions of our tests the Oxford staphylococcus was inhibited by 0·1 unit of penicillin per ml. of medium. This relatively high reading may be associated with the size of the inoculum used in our tests; with 1/500 of this inoculum the reading was 0·05 unit per ml. In two small batches of strains of *C. diphtheriæ* tested in two different laboratories where the bacteriostatic levels for the strains of *C. diphtheriæ* were above the average the Oxford staphylococcus was inhibited by 0·2 unit of penicillin, but the ratio was normal. Though it is necessary to mention these few discrepant results, the findings in the different laboratories were remarkably uniform. The results (tables I and II) show that gravis strains of *C. diphtheriæ* are rather more resistant to penicillin than intermedius, and that intermedius are more resistant than mitis strains. It is also clear that most of the strains tested required two or three times as much penicillin for in-vitro inhibition as did the standard strain of staphylococcus.

TREATMENT OF ACUTE CASES

All patients with acute diphtheria received antitoxin in doses depending on the severity of the case. A single batch of crystalline penicillin (sodium salt) was used to treat most of the cases. The standard adult dose was 60,000 units given intramuscularly four-hourly during the day-time only (daily dosage 240,000 units). Children aged 0–4 years received a third, and children aged 5–10 years two-thirds, of the adult dose. Children over 10 years were treated as adults.

A bacteriological check was kept on acute cases by swabbing the nose and throat every other day during

TABLE II—PENICILLIN-SENSITIVITY OF 284 STRAINS OF *C. diphtheriæ* EXPRESSED AS A RATIO* OF THE SENSITIVITY OF THE OXFORD STAPHYLOCOCCUS

Ratio	All strains	Gravis	Intermedius	Mitis
10	2	2	—	—
6	22	12	3	7
3	75	36	18	21
2	125	40	27	58
1	38	4	12	22
0·6	14	1	2	11
0·3	8	—	—	8
Totals ..	284	95	62	127
Arithmetic mean	2·33	2·85	2·25	1·99
Geometric mean ..	—	0·270	0·206	0·165

* Ratio was obtained by the quotient:
Units of penicillin per ml. of broth bacteriostatic for *C. diphtheriæ*
Units of penicillin per ml. of broth bacteriostatic for Oxford staphylococcus

* Dr. ROBERT CRUICKSHANK, Dr. E. H. GILLESPIE, Dr. WILLIAM GOLDIE, Dr. H. J. HARRIS, Dr. W. H. H. JEBB, Dr. G. J. G. KING, Dr. P. H. MARTIN, Dr. M. T. PARKER, Dr. ALEXANDER MACDONALD (secretary).
† Cardiff, Carmarthen, Ipswich, Leicester, London, Northallerton, Norwich, and Oxford.

Digitized by Google

TABLE III—RESULTS OF TREATMENT OF ACUTE CASES OF DIPHTHERIA WITH PENICILLIN

Type of *C. diphtheriæ*	No. of cases treated	Proportion of cases treated "successfully"*		No. in which treatment failed
		Three days	Six days	
Gravis ..	29	7/14	12/15	10
Intermedius ..	17	9/12	3/5	5
Mitis	19	10/11	8/8	1
Totals ..	65	26/37	23/28	16

* "Successful" = no positive swab later than four days from the end of penicillin therapy.

treatment and for a week thereafter. Subsequent swabs were taken at weekly intervals until the patient was discharged from hospital. All swabs were plated on tellurite medium and examined after twenty-four and forty-eight hours in the incubator.

The cases were divided into two groups: one received treatment for three days only, and the other for six days. Treatment with penicillin was considered successful if the patient had the first of a series of consistently negative swabs within four days of the end of the penicillin course. Results are shown in table III and compared in the figure with Wright's (1941) series in Liverpool.

Because of the very few cases available in most of the laboratory areas it was impossible to treat alternate cases with antitoxin alone. At one centre, however, 6 out of 13 cases were "successfully" treated with a three-day course of penicillin, whereas only 3 of 22 control cases treated in the same hospital with antitoxin alone had the first of a series of consistently negative swabs within a fortnight of admission.

TREATMENT OF PERSISTENT CARRIERS

For the purposes of the investigation a persistent carrier was defined as one known to have carried *C. diphtheriæ* in his throat for at least six weeks. Most of the carriers treated were not known to have had acute diphtheria, but a few were considered to be persistent carriers if after six weeks in hospital for acute diphtheria they still harboured the organism in large numbers. At first penicillin treatment for throat carriers was given in the same doses as for acute cases. Later the dose of penicillin was increased to 500,000 units twice daily for three days. Throat and nose swabs were bacteriologically examined as for acute cases, and the test of successful treatment was the same. The results are shown in table IV.

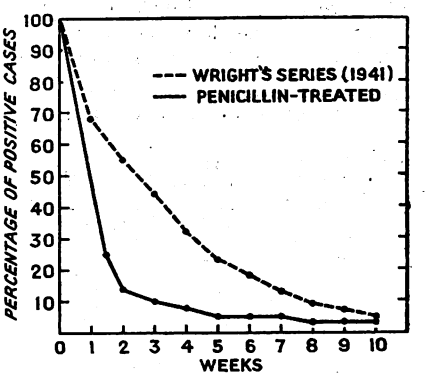
TABLE IV—RESULTS OF PARENTERAL PENICILLIN TREATMENT OF DIPHTHERIA THROAT CARRIERS

Type of *C. diphtheriæ*	No. of cases treated	"Successfully" treated	Failures
Gravis	14	3	11
Intermedius ..	3	2	1
Mitis	14	8	6
Totals ..	31	13	18

Most of the carriers treated with the same doses as acute cases were given a six-day course; but 9 carriers were given 500,000 units of penicillin twice a day for three days, with 3 successes and 6 failures, 5 of the failures being of the gravis type. Sensitivity tests were performed on 5 strains of *C. diphtheriæ* (4 gravis and 1 intermedius) isolated from carriers before and after penicillin treatment. None of the strains isolated after treatment showed an increased resistance to penicillin in the test-tube. Among the 18 carriers in whom treatment failed 7 were known to have diseased tonsils and of these 5 later had their tonsils removed, with subsequent cure of the carrier state. Besides the carriers listed in table IV, 2 nasal carriers were treated successfully with intramuscular penicillin for three days; 3 further cases of anterior nasal diphtheria were treated three-hourly with a local spray of penicillin solution containing a daily dose of 100,000 units. Treatment was given for three days and all 3 cases satisfied the criterion of cure.

COMMENT

Though penicillin-sensitivity tests are done routinely in many laboratories, we found it at first extremely difficult, even with a relatively simple culture medium, to achieve a technique which would ensure results quantitatively uniform from one laboratory to another. Preliminary investigation was carried out on such factors as the size of inoculum, the sample and preparation of horse serum used, clumping of certain strains of the diphtheria bacillus, and the method of reading end-points. When these difficulties had been overcome, most of our strains of *C. diphtheriæ* were finally tested in two laboratories, and the results were very uniform.



Rate of disappearance of *C. diphtheriæ* in cases of faucial diphtheria treated with penicillin.

Most of the strains required two or three times as much penicillin for inhibition as does the Oxford staphylococcus. Only 2 strains were encountered which had a ratio greater than six. From table II statistical analysis has shown that the differences in the mean sensitivity of each of the three types are all significant, and there is little doubt that the gravis strains are more resistant to penicillin than the mitis type. The scatter of the sensitivities of the three types, as measured by standard deviations, shows that the mitis type differs significantly from intermedius and gravis. This greater scatter of the resistance of the mitis type of *C. diphtheriæ* is perhaps understandable in view of the greater biological variation in this group of strains. The results, however, make it clear that strains of *C. diphtheriæ* of all three types tested are sensitive in vitro to concentrations of penicillin which can readily be reached in the body.

Because of the limited number of cases and carriers at our disposal we could not carry out the type of trial of penicillin treatment which is obviously required. The rate of elimination of *C. diphtheriæ* from the nose or throat of patients may depend on several variables, such as the type or even the strain of *C. diphtheriæ*, the state of the patient's tonsils, his age, and whether or not he has been immunised. We have treated sporadic cases of diphtheria in different parts of the country, and our results may therefore not be strictly comparable with those of other workers. Table III shows that 75% of 65 acute cases treated with penicillin were free of the infecting organism within ten days of starting treatment, and that 26 (70%) of 37 acute cases treated for three days had become bacteriologically negative within a week.

In the figure we have compared Wright's (1941) Liverpool series of cases of acute diphtheria treated with antitoxin alone with our penicillin-treated cases. Only 45% of Wright's cases were bacteriologically negative fourteen days after admission to hospital, compared with 86% of our penicillin-treated cases. Wright's figures show differences in the rate of clearance of the three types of *C. diphtheriæ* from the nose and throat of acute cases,

Digitized by Google

the gravis type tending to persist longer than mitis or intermedius. This suggests that the precise rate of disappearance of *C. diphtheriæ* in any series of cases will be influenced by the type composition of that series. In comparing our results with those obtained at Liverpool it must also be remembered that the two sets of figures were obtained at very different times, and that our curve is based on only a fifth of the number of cases examined by Wright. It is also possible that cross-infection may have prolonged the carrier state in some of Wright's cases, though his investigation deals with the type with which the patient was originally infected. However, Wright's findings in children are essentially similar to those obtained by Hartley and Martin (1919–20) in soldiers and by Thomson et al. (1926–27) in a London fever hospital. Wright's curve being taken as an adequate basis for comparison, the curve for the rate of disappearance of *C. diphtheriæ* in penicillin-treated cases falls much more steeply. Our series included a proportion of immunised patients, but there was no evidence that immunisation affected the clearance-rate.

Wright's finding and our own small group of control cases support the view that penicillin treatment shortens the duration of carriage of *C. diphtheriæ* in acute cases, and that our results would not have been obtained in cases treated with antitoxin alone. The small group of cases caused by the mitis type of *C. diphtheriæ* appeared to respond best to penicillin treatment. Apart from any possible clinical benefit which penicillin treatment may confer, the early elimination of *C. diphtheriæ* is desirable to reduce the risk of cross-infection and, in many instances, to shorten the patient's stay in hospital.

Penicillin treatment of persistent carriers has not, in the doses used, given very encouraging results, but the number of carriers treated was too small for definite conclusions to be drawn. Of 31 carriers treated 13 appeared to respond to penicillin, but possibly some of these would have become clear spontaneously during the period of test. The higher doses of penicillin advocated by Long (1947) apparently gave in a few of our carriers no better results than the smaller doses used earlier. Our records suggest that it may well be easier to prevent with penicillin the acute case from becoming a convalescent carrier than to cure the established carrier condition. If this is so, there is every reason to begin penicillin therapy as early in the disease as possible and not to wait until the diphtheria organism has become firmly established in diseased tonsils.

SUMMARY

Penicillin-sensitivity tests were carried out on 284 strains of *C. diphtheriæ* isolated in different parts of the country. Most of the strains tested were two or three times as resistant to penicillin as the Oxford staphylococcus. Gravis strains of *C. diphtheriæ* were more resistant to penicillin than intermedius, and intermedius were more resistant than mitis types.

Of 65 acute cases of faucial diphtheria treated with penicillin, 26 of 37 receiving a three-day course, and 23 of 28 receiving a six-day course, became free from the infecting organism within four days of the end of treatment. In 31 persistent diphtheria carriers penicillin treatment was followed by the rapid disappearance of the organism from the throat in only 13 cases.

We wish to thank Dr. Joseph Ungar, of Glaxo Laboratories, for supplying the penicillin for sensitivity tests; and numerous medical officers of health and clinicians who treated the cases and carriers.

REFERENCES

Hartley, P., Martin, C. J. (1919–20) *Proc. R. Soc. Med.* **13**, 277.
Karelitz, S., Wasserman, L. R., Moloshok, R. E. (1947) *J. Pediat.* **30**, 18.
Long, D. A. (1947) *Brit. med. J.* i, 884.
Thomson, F. H., Mann, Elsie J., McCartney, J. E., Harvey, W. C. (1926–27) Metropolitan Asylums Board Annual Report, p. 214.
Wright, H. D. (1941) *J. Path. Bact.* **52**, 129.

THYMINE, FOLIC ACID, AND VITAMIN B_{12} IN NUTRITIONAL MACROCYTIC ANÆMIA, TROPICAL SPRUE, AND PERNICIOUS ANÆMIA*

TOM D. SPIES
M.D. Harvard

HEAD OF DEPARTMENT OF METABOLISM AND NUTRITION, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO; DIRECTOR, NUTRITION CLINIC, HILLMAN HOSPITAL, BIRMINGHAM, ALA.

ROBERT E. STONE
M.D. Harvard

ASSOCIATE DIRECTOR, NUTRITION CLINIC, HILLMAN HOSPITAL

GUILLERMO GARCIA LOPEZ
M.D. Havana

FERNANDO MILANES
M.D. Havana

ASSOCIATE PROFESSORS OF GENERAL PATHOLOGY, UNIVERSITY OF HAVANA

RUBEN LOPEZ TOCA
M.D. Havana
INSTRUCTOR IN GENERAL PATHOLOGY, UNIVERSITY OF HAVANA

TOMAS ARAMBURU
M.D. Havana
WILLIAMS-WATERMAN FELLOW IN NUTRITION

THE rapidity with which the scientific and therapeutic advances on folic acid or pteroylglutamic acid (Spies 1947), thymine or 5-methyl uracil (Spies et al. 1946), and vitamin B_{12} (West 1948, Spies et al. 1948a and b) have been made is unparalleled. Within three years these three compounds have been found to produce blood regeneration in certain types of macrocytic anæmia. Each has offered the prospect of specific therapy with a pure chemical compound. The molecular structures of thymine and of folic acid are known, and much work is being done to elucidate the structure of vitamin B_{12}.

Under the scrutiny of physicians these materials must be appraised in respect to their effect on man. It is well known that the response of patients to liver extract or to folic acid is extremely variable. Some respond maximally to much smaller doses than do others. This extreme variation in the individual response under test conditions made it desirable to observe the effect of folic acid, thymine, and vitamin B_{12} in the same person in the same degree of relapse, under similar conditions, and on the same diet. The present report is limited to a study of the blood response to each of these substances in a patient with nutritional macrocytic anæmia, one with pernicious anæmia, and one with tropical sprue.

Using the diagnostic criteria and laboratory methods previously described (Spies 1947), we selected and studied three patients. Each was admitted to hospital in relapse three times and on each admission was given a different pure chemical substance, while the diet and the conditions of the study were kept constant.

CASE-RECORDS

Case 1.—A white man, aged 51, was admitted to the Jefferson-Hillman Hospital, Birmingham, Alabama, in April, 1946, complaining of extreme weakness. His family history and previous personal history were irrelevant. Three years before admission, while working as a coalminer, he developed shortness of breath, tinnitus, vertigo, "fluttering of the heart," "shimmering of the vision," and frequent bleeding of the gums. These symptoms progressed rapidly, and within two months of their onset the patient was forced to stop working and was admitted to a hospital, where he was treated with liver extract. He soon became asymptomatic and was discharged from the hospital. On returning home he resumed eating the same type of diet he had eaten as long as he could remember. It consisted of grits, bread, syrup, fat, two eggs, and two glasses of milk daily. He rarely ate meat,

* Northwestern University studies in nutrition at the Hillman Hospital, Birmingham, Alabama, and at the General Calixto Garcia Hospital, Havana, Cuba.

Digitized by Google

poultry, cheese, green vegetables, or fruit. Fig. 1 shows that his diet was deficient in many nutrients, particularly nicotinic acid and ascorbic acid. Except for moderate weakness he remained well until April, 1946, when he developed moderately severe diarrhœa and his weakness became severe. At that time he came to the nutrition clinic seeking treatment and was admitted to the hospital.

First Admission.—He was pale and seemed weak but not acutely ill. His skin was very pale and slightly icteric. The skin on the dorsum of the hands was moderately thickened, pigmented, furrowed, and inelastic. On the elbows, across the scapulæ and spine, and round the ankles the skin was thickened and wrinkled. The palpebral conjunctivæ were moderately pale. There was bilateral generalised injection of the ocular conjunctivæ. In each eye, on the nasal side, there was a severely injected pterygium, which extended on to the cornea. The buccal mucosa was pale and œdematous. The nail beds were extremely pale. Neurological examination showed nothing abnormal.

Gastric analysis showed free hydrochloric acid in the gastric contents. Gastro-intestinal radiography was negative. An oral glucose-tolerance test showed a normal curve. The urine was normal. The stools contained no ova, parasites, occult blood, or urobilin. The icteric index was 10·9 units. The red-cell count was 2,220,000 per c.mm., Hb 10·7 g. per 100 ml. (70%), and reticulocytes 2·4%. The sternal bone-marrow showed typical megaloblastic arrest. Nutritional macrocytic anæmia was diagnosed.

The patient was kept on a diet devoid of meat and meat products. After the base-line studies had been completed, he was given 6 g. (6,000,000 μg.) of synthetic thymine daily by mouth for fourteen days. The blood response is shown in fig. 2. The patient's strength gradually returned as his blood-levels rose and his diarrhœa subsided. When he was discharged from hospital three weeks after admission he volunteered that he felt better than he had for many months.

Second Admission.—He remained well until January, 1947, when he began having occasional diarrhœa, with watery stools, soreness of the tongue, bleeding of the gums, and a recurrence of weakness. On his second admission to the hospital his red-cell count was 2,170,000 per c.mm., Hb 8·8 g. per 100 ml. (58%), and reticulocytes 1·4%. The results of gastric analysis, glucose-tolerance test, stool studies, analysis of urine, and sternal bone-marrow study were essentially the same as on his previous admission.

He was given 10 mg. (10,000 μg.) of synthetic folic acid daily by mouth for ten days. The blood response is shown in fig. 2. His diarrhœa stopped six days after the start of therapy. He gained strength rapidly and was discharged two weeks after admission.

Third Admission.—In April, 1948, the patient rather suddenly developed anorexia, general weakness, and slight soreness of the mouth and tongue. These symptoms progressed rapidly for a week, and he came to the nutrition clinic. On his third admission his red-cell count was 2,020,000 per c.mm., Hb 6·5 g. per 100 ml. (42%), reticulocytes 3·6%. The results of gastric analysis, glucose-tolerance test, stool studies, and urine analysis were essentially unchanged. Physical examination revealed nothing remarkable except a more severe glossitis than had been observed during any previous relapse of his anæmia.

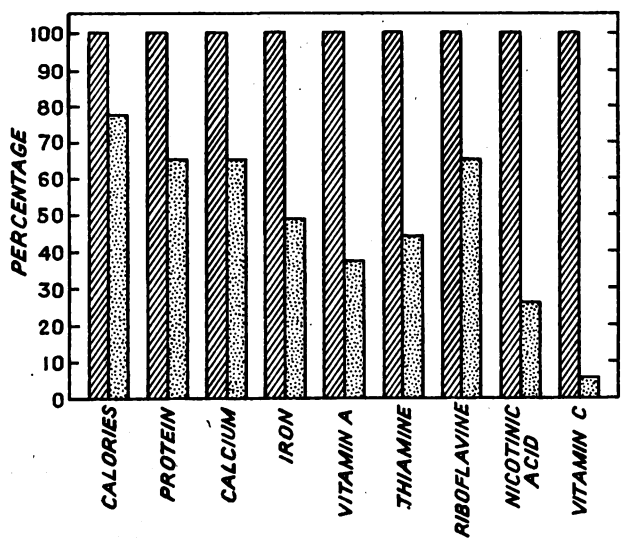


Fig. 1—Comparison of diet of case 1 (stippled columns) with diet recommended by National Research Council (hatched columns). The only animal protein eaten by the patient came from milk and eggs.

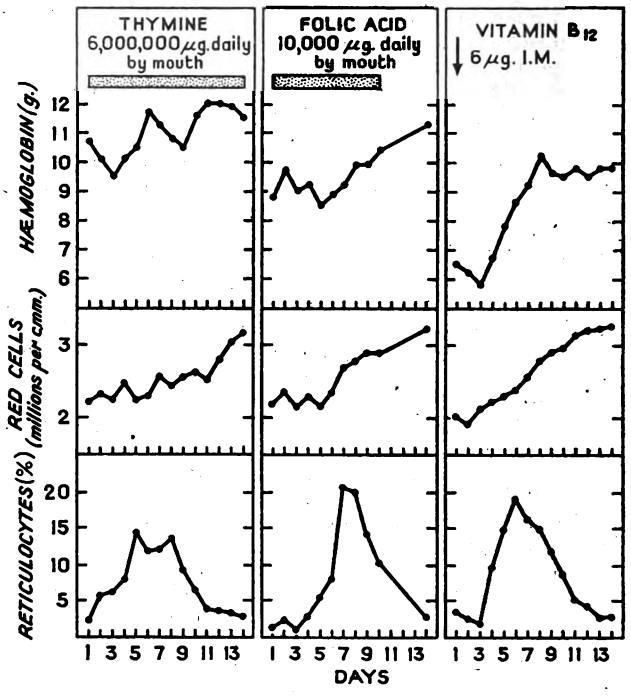


Fig. 2—Blood responses of case 1.

The patient was given a single injection of 6 μg. of vitamin B_{12} intramuscularly. The blood response is shown in fig. 2. The glossitis had disappeared by the fifth day after the injection, and he quickly and steadily gained strength.

Case 2.—A white Cuban farmer, aged 70, was admitted to the General Calixto Garcia Hospital, Havana, in May, 1946, complaining of loss of appetite, diarrhœa, and weakness. His family history and previous personal history were irrelevant. Four months before admission he began to have diarrhœa, consisting of 6–8 large watery yellow foamy stools daily. Within a week his bowel movements increased to 11 or 12 daily; his tongue became very sore, and he began to have severe epigastric distress. He was unable to eat anything but rice, soup, and milk. Ten days after his illness began, weakness forced him to stop work; and from then until he was admitted to hospital he spent most of the time in bed. During the four months he lost 40 lb. in weight.

First Admission.—He was pale and looked very weak and ill. His skin was generally pale. His tongue was red and slick. The buccal mucosa, conjunctivæ, and nail beds were very pale. There were no other abnormal physical findings, and neurological examination was negative.

Gastric analysis showed free hydrochloric acid in the gastric contents. The stools were voluminous, liquid, foul-smelling, and whitish-yellow; they contained no ova, parasites, occult blood, or urobilin. On gastro-intestinal radiography the barium column was not continuous but broken into many isolated areas. An oral glucose-tolerance test showed a flat curve. The sternal bone-marrow showed typical megaloblastic arrest. The red-cell count was 2,390,000 per c.mm., Hb 9·3 g. per 100 ml. (60%), and reticulocytes 2·8%. Tropical sprue was diagnosed.

The patient was kept on a diet devoid of meat and meat products throughout. After the base-line studies had been completed he was given 10 g. (10,000,000 μg.) of synthetic thymine by mouth daily for fourteen days. The blood response is shown in fig. 3. Clinical improvement began three days after therapy was started; his appetite improved, and he said he felt stronger. By the end of the first week he was spending most of the day out of bed. The diarrhœa began to subside about this time; the stools became fewer and better

Digitized by Google

formed. Improvement continued, and he was discharged three weeks after admission. Gastro-intestinal radiography a month after therapy showed a continuous barium column.

Second Admission.—He remained well until April, 1947, when he again began to have diarrhœa and loss of appetite. He was visiting in the country at the time and did not come to the hospital until a month after the onset of these symptoms. On his second admission the clinical and laboratory findings were similar to those on his previous admission, except that the red-cell count was 1,170,000 per c.mm., Hb 5·1 g. per 100 ml. (33%), and reticulocytes 2·2%.

He was given 10 mg. (10,000 μg.) of synthetic folic acid by mouth daily for fourteen days. The blood response is shown in fig. 3. Clinical improvement began about the time the reticulocytes began to rise on the fourth day of therapy; the soreness of his tongue was relieved, his appetite returned, and he began to get stronger. By the ninth day of therapy his bowel actions had decreased from 10 to 3 daily, and the stools were better formed and more normal in colour. By the time he was discharged, three weeks after admission, he had gained 10 lb. and felt well.

Third Admission.—He had no recurrence of symptoms until May, 1948, when he developed severe bronchitis and lost his appetite. Within a week of the onset he began having moderately severe diarrhœa, soreness of the tongue, and epigastric distress. He was in bed and unable to come to the hospital for four weeks after he became ill. When he came and was admitted for the third time his tongue was moderately reddened; he was very pale and weak and was having 4 or 5 soft or liquid yellowish-brown stools daily. His red-cell count was 2,500,000 per c.mm., Hb 7·8 g. per 100 ml. (50%), and reticulocytes 1%. The other laboratory findings were as on his first admission.

He was given a single injection of 23 μg. of vitamin B_{12}. The blood response is shown in fig. 3. His appetite improved and he felt well four days after therapy, and he steadily gained in strength. Eight days after therapy his bowel movements decreased to 2 soft fairly well-formed stools daily.

Case 3.—A white man, aged 46, was admitted to the Hillman-Jefferson Hospital, in March, 1946, complaining of general weakness, dyspnœa, palpitation on exertion, soreness of the mouth and tongue, swelling of the legs and feet, and paræsthesiæ of the extremities. His family history and previous personal history were irrelevant. A year before his admission he noted that he became tired very easily, had difficulty in breathing, and had palpitation on exertion. These symptoms gradually became more severe. Six months after their onset his tongue, which he had noted to be abnormally red, began burning, especially when he ate "sour or hot" foods. About three months later he began to have numbness of his hands and feet and swelling of his feet and ankles.

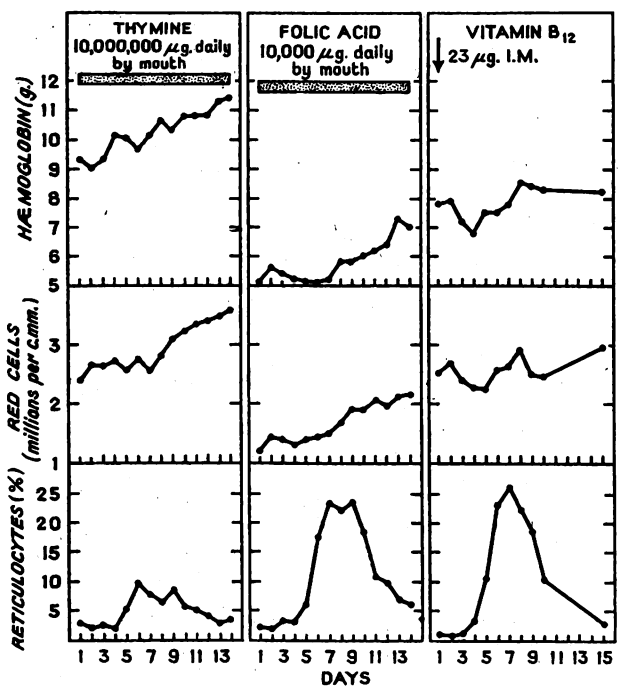


Fig. 3—Blood responses of case 2.

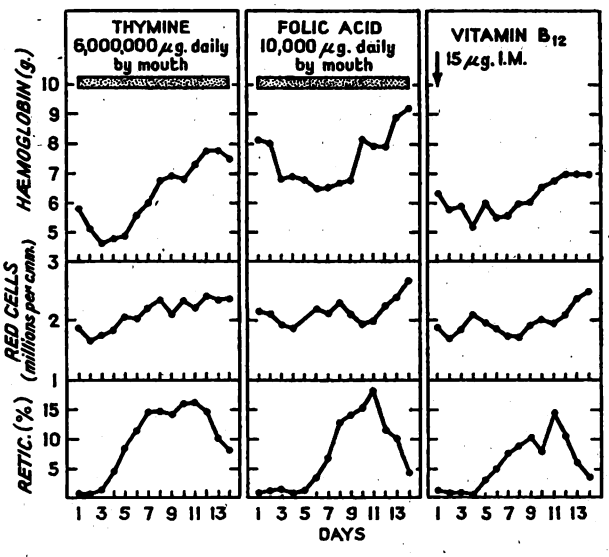


Fig. 4—Blood responses of case 3.

First Admission.—He was pale and looked weak but not acutely ill. The skin, nail beds, and conjunctivæ were very pale. His tongue was smooth and red; the buccal mucosa was red, and the gums were swollen and injected. Neurological examination showed sensory changes suggesting peripheral neuritis.

Gastric analysis showed no free hydrochloric acid after histamine stimulation. Gastro-intestinal radiography was normal. An oral glucose-tolerance test showed a flat curve. The urine was normal. The stools contained no ova, parasites, or occult blood. The red-cell count was 1,860,000 per c.mm., Hb 5·8 g. per 100 ml. (38%), and reticulocytes 0·3%. The sternal bone-marrow showed typical megaloblastic arrest. Pernicious anæmia was diagnosed.

The patient was kept on a diet devoid of meat and meat products. After the base-line determinations had been completed, he was given 6 g. (6,000,000 μg.) of synthetic thymine by mouth daily for fourteen days. The blood response is shown in fig. 4. Though the sternal bone-marrow just after the peak of reticulocytosis revealed a normoblastic reactive stage, his anæmia began to relapse soon after therapy was discontinued. Clinically his improvement was slight; the stomatitis, the glossitis, and the nervous symptoms did not improve.

Second Admission.—In December, 1946, the weakness and dyspnœa recurred, but he did not come to the clinic until May, 1947, when he had become too weak to continue working. On his second admission the physical findings were essentially the same as on his previous admission. His red-cell count was 2,150,000 per c.mm., Hb 8·1 g. per 100 ml. (53%), and reticulocytes 0·6%. The other laboratory findings were as on his first admission.

He was given 10 mg. (10,000 μg.) of synthetic folic acid daily by mouth for ten days. Fig. 4 shows his blood response. As his blood-levels rose he gained strength, and the glossitis and stomatitis improved, though they did not disappear entirely.

Third Admission.—In March, 1948, the patient developed very severe glossitis, stomatitis, and weakness, and was admitted for the third time. His red-cell count was 1,090,000 per c.mm., Hb 6·3 g. per 100 ml. (41%), and reticulocytes 1%.

He was given a single injection of 15 μg. of vitamin B_{12} intramuscularly. His blood response is shown in fig. 4. Definite fading of the hyperæmia of the tongue and the mucosa of his mouth was observed forty-eight hours later. Five days after the injection of vitamin B_{12} the colour of the mucosa was almost normal. Regeneration of the lingual papillæ was apparent by the thirteenth day. A remarkable improvement in his strength and vigour paralleled his blood response.

Digitized by Google

SUMMARY AND CONCLUSIONS

A comparative study of thymine, folic acid, and vitamin B_{12} has been made under controlled conditions on selected patients with macrocytic anæmia in relapse. One patient with pernicious anæmia, one with nutritional macrocytic anæmia, and one with tropical sprue were each admitted three times to the hospital and given a diet free from meat and meat products. Base-line determinations were made on each admission. Each compound produced a blood response and a definite clinical improvement.

The fact that three distinct chemical compounds have proved effective in each of three distinct syndromes suggests that we may learn a great deal about the pathogenesis of these diseases.

From these and other studies by us it appears that several thousand times the weight of thymine is required to produce a response similar to that produced by folic acid, and that several thousand times the weight of folic acid is required to produce a response similar to that produced by vitamin B_{12}. These findings suggest that vitamin B_{12} is by far the most potent antianæmic substance known.

This work was aided by grants from the Martha Leland Sherwin Memorial Fund, the Birmingham Citizens Committee, and the Fundacion de Investigaciones Medicas of Havana, Cuba.

The thymine was supplied by Dr. J. A. Aeschlimann, of Hoffmann-LaRoche Inc.; the folic acid by Dr. Benjamin Carey and Dr. Stanton Hardy, of Lederle Laboratories Inc.; and the vitamin B_{12} by Dr. Augustus Gibson, of Merck and Company, Inc.

REFERENCES

Spies, T. D. (1947) Experiences with Folic Acid. Chicago.
— Frommeyer, W. B. jun., Vilter, C. F., English, A. (1946) *Blood*, **1**, 185.
— Garcia Lopez, G., Milanes, F., Lopez Toca, R., Culver, B. (1948a) *Sth. med. J.* **41**, 523.
— Stone, R. E., Aramburu, T. (1948b) *Ibid*, p. 522.
West, R. (1948) *Science*, **107**, 398.

EXCHANGE TRANSFUSION IN HÆMOLYTIC DISEASE OF THE NEWBORN

P. L. MOLLISON, M.D. Camb., M.R.C.P.
M. CUTBUSH, B.Sc. Melb.

From the Medical Research Council Blood Transfusion Research Unit, Department of Obstetrics, Postgraduate Medical School of London

IN 1946 Wallerstein pointed out that the treatment of hæmolytic disease by repeated transfusion of Rh-negative blood did not prevent some infants from dying of "toxæmia," and he suggested that withdrawal of part of the infant's blood, with simultaneous replacement by Rh-negative blood, might be more successful by removing end-products of red-cell breakdown. He found that, if 250 ml. of the infant's blood was withdrawn from the sagittal sinus, and 250 ml. of Rh-negative blood simultaneously transfused into a peripheral vein, about a 65% replacement of blood was achieved.

Wiener and Wexler (1946) introduced the modification of bleeding the infant from the radial artery; they considered mathematically the effect on the composition of the infant's blood of simultaneous bleeding and withdrawal, and plotted a curve showing the percentage exchange after the withdrawal and injection of increasing amounts of blood. They concluded that, if the exchange were continued until an amount equivalent to twice the infant's initial blood volume—i.e., 2 × 250 ml.—had been withdrawn and replaced by Rh-negative blood, 86% of the cells remaining in the infant's circulation should be Rh-negative. Wiener et al. (1948) have since suggested that even more massive replacements should be performed, and state that an exchange of 1000 ml. leads to a replacement of about 98% of the infant's red cells.

MECHANISM OF TISSUE DAMAGE

Discussion of the treatment of hæmolytic disease of the newborn is greatly handicapped by the lack of any real understanding of the mechanism of the damage to the brain and liver which occurs in some cases and causes all the unpleasant sequelæ and many of the deaths. Clearly, if this damage were fully established at birth, little could be hoped for from subsequent treatment. Vaughan (1946) and Parsons (1947) have drawn attention to the fact that infants who develop damage to the liver and brain tend not to show any pronounced anæmia, and this has led them to conclude that the damage may be due to a direct action of antibody on the tissues rather than to any indirect effect of blood destruction. However, the matter remains controversial, and the following points may put the above-mentioned observations in a slightly different light.

First, though anæmia can be readily diagnosed by examining cord blood, in which the range of normal values is fairly narrow, it is far harder to interpret hæmoglobin estimations made in the few days after birth. It is now accepted that at birth the infant receives a variable amount of blood from the placenta according to the time at which the cord is tied, and that this leads to a variable increase in hæmoglobin values after birth (DeMarsh et al. 1942). This widens the normal range of values and may mask a moderate anæmia. We have observed that an infant whose cord blood contains a concentration of hæmoglobin well below the normal range may receive a sufficient amount of blood from the placenta to acquire a value, a few hours after birth, which lies within normal limits. Thus a normal hæmoglobin value during the first day or two of life can certainly not by itself be taken as excluding the operation of a hæmolytic process.

Secondly, even the maintenance of a high hæmoglobin value for many days after birth does not preclude the possibility that a very rapid destruction of blood is being fully compensated by a rapid regeneration. We have observed a case in which an infant with very deep jaundice maintained a hæmoglobin value of 120% between the 4th and 7th days of life but was found by cell-survival experiments to be destroying 50% of transfused Rh-positive cells in two days.

Thirdly, in our experience, infants who are profoundly anæmic at birth are likely to die within 24 hours; doubtless many are stillborn. Thus there is a tendency for infants who are severely anæmic at birth not to live long enough to develop kernicterus.

These three points make it possible that tissue damage may, after all, prove to be specially associated with rapid blood destruction. That anti-Rh has a direct action on the tissues of a Rh-positive infant seems doubtful, since we have sometimes observed a large amount of free Rh-antibody persisting in the plasma of an affected infant for many weeks after treatment by a simple transfusion, without the development of any signs of damage to the liver or the brain.

It remains doubtful whether the tissue damage sometimes associated with hæmolytic disease is established at birth, and we believe there is some evidence that it may, at least sometimes, mainly occur after birth. It is possible that the poor excretory capacity of the liver in the first few days of life is concerned, and it is of some interest that deaths from the "toxic stage" of hæmolytic disease take place at 2–4 days, just when physiological hyperbilirubinæmia in the normal newborn infant is at its highest. At all events there is sufficient doubt about the cause of deaths at 2–4 days to make it worth while to try the effect of removing as many as possible of the Rh-positive cells very soon after birth and replacing them by Rh-negative cells by exchange transfusion.

Digitized by Google

It is known that, if the infant is provided with a sufficiently high concentration of Rh-negative cells, Rh-positive cells fall to a low level or disappear completely for a while, evidently because the stimulus to the production of new cells has been removed (Mollison 1943). Simple transfusion of Rh-negative cells will thus also lead to a replacement of Rh-positive cells by Rh-negative cells but will leave the infant to excrete a far larger number of Rh-positive cells.

CORRECTION OF ANÆMIA

In discussing the treatment of hæmolytic disease of the newborn the impression must not be given that prevention of tissue damage is the only object of treatment. Some deaths take place within 24 hours of birth, and we believe that the mechanism in this group of early deaths is different. Those infants who die soon after birth are all profoundly anæmic and are usually cyanosed. In a few cases in which we have measured the venous pressure we have found it strikingly increased. It seems likely that the syndrome displayed by this group of cases is similar to the "hyperkinetic phase" described by Howarth and Sharpey-Schafer (1947) in adults with chronic severe anæmia. In this group the object of treatment must be to raise the hæmoglobin without overloading the circulation, and this can be most rationally accomplished by exchange transfusion. Nevertheless the prognosis in these cases is very bad, and no form of treatment is likely to save many of them; there seems little doubt that they can be regarded as border-line cases of hydrops fœtalis.

Infants who survive the first five days of life without showing any signs other than jaundice and perhaps some pallor may later develop profound anæmia and need one or more transfusions. If exchange transfusion could be as simply carried out, and be shown to be as safe, as an ordinary transfusion, it might prove to be the most satisfactory method of treatment for all cases of hæmolytic disease other than the mildest.

With the introduction by Diamond (1947) of the technique of carrying out exchange transfusions through a plastic catheter passed up the umbilical vein after birth, we felt that the needed simplification in technique had been achieved, and since March, 1947, we have given this method a fairly extensive trial.

METHODS

Selection of Cases

The cases were selected from 63 infants seen by us in 1½ years. All these 63 infants were Rh-positive and were born to women whose sera contained Rh-antibody. The 33 infants not treated by exchange transfusion via the umbilical vein included 6 born dead or moribund, 13 treated by simple transfusion of Rh-negative blood into a peripheral vein, and 14 so mildly affected as to require no treatment.

Whenever possible, cord blood was examined. Otherwise a venous sample was taken as soon after birth as possible. The main examinations made were a direct Coombs test, hæmoglobin, plasma-bilirubin, degree of erythroblastæmia, and amount of free antibody. As the investigation proceeded, it became clear that it was possible to make reliable estimates of severity as a result of these examinations, and we left untreated any infant whom we considered was mildly affected and unlikely to need a transfusion subsequently.

The 30 infants selected for exchange transfusion were all infants whose cord blood had either a hæmoglobin below the normal range, or a bilirubin value above the normal range, or both. Further details are given below.

Technique

We have described elsewhere the technique of exchange transfusion via the umbilical vein (Mollison, Mourant, and Race 1948). This technique is based on that described by Diamond (1947), though it is not known whether it differs from his in minor details.

The essentials of the technique are as follows:

Under aseptic conditions the umbilical cord is completely divided about ½ in. from the abdominal wall. A fine transparent plastic catheter is passed up the umbilical vein until blood can be freely withdrawn (usually 2–3 in.), whereupon 20 ml. of blood is withdrawn and immediately replaced by 20 ml. of Rh-negative blood. An arrangement of stopcocks makes it possible to do this without changing the syringe. Thus 20 ml. amounts of blood are exchanged until about 350–450 ml. has been withdrawn and replaced by Rh-negative blood. In some cases an additional 50 ml. of blood is finally injected without any further withdrawal.

The whole procedure takes 1 or 2 hours. No heparin is injected into the infant, but the apparatus is rinsed with dilute heparin-saline solution from time to time.

The exchange transfusions were most often carried out within 13 hours of birth (23 cases). In the remaining 7 cases they were done 17–38 hours after birth. Occasionally in these later cases small clots were found in the umbilical vein, but these did not obstruct the passage of the catheter. In most cases there was no special difficulty in passing the catheter, once practice had been acquired.

We have used umbilical catheterisation for obtaining blood samples or carrying out tests on other infants, so that in all we have used this method in 77 cases. Though in the first few weeks, when we were acquiring experience with this method, we twice failed to pass the catheter we have since only once been unsuccessful. In this series of 77 cases we have not seen any umbilical sepsis, though only about 7 of the infants having exchange transfusions and none of the infants having simple tests were given prophylactic chemotherapy. Nevertheless, until experience has been acquired, we recommend that the infants be given prophylactic doses of penicillin for 48 hours.

In this series we have not seen any ill effects attributable to the procedure. One infant bled from the cord some hours later, but the hæmorrhage seemed to be coming from a small vessel and not from either of the umbilical arteries or the umbilical vein, and it seemed that the hæmorrhage might well have occurred in any event, simply from the unusual vascularity of the cord. Air-embolism has been reported as a danger of this method, but in the case concerned a rubber catheter was used (J. J. Van Loghem, personal communication). With the transparent polyethylene catheter that we have used throughout, minute air-bubbles can easily be seen and their introduction into the infant's circulation readily avoided.

Choice of Donor

At first ordinary stored blood was used, but it soon became clear that it had the disadvantage of being too greatly diluted with citrate. Subsequently, therefore, slightly concentrated suspensions of red cells were prepared by removing some of the supernatant plasma-citrate immediately before use. Whenever possible, donors were bled specially into relatively small volumes of anticoagulant. It was found convenient to use the mixture recommended by Ross et al. (1947)—i.e., disodium citrate 2·5 g., glucose 3 g. made up in 50 ml. of distilled water—and 500 ml. of blood was taken into a bottle containing this mixture. Alternatively the donor was bled into a bottle containing 1–2 ml. (2000 Toronto units) of heparin.

When supernatant plasma-citrate was removed, we were often left with only 400 ml. of donor's blood or even less. However, we found that, provided we had raised the red-cell count of the modified donor's blood to between 5 and 6 million red cells per c.mm., the injection of 300–400 ml. usually achieved at least an 85% exchange of red cells. Provided that the infant showed no sign of circulatory overloading, which we sometimes checked by direct measurement of venous

Digitized by Google

pressure through the umbilical catheter, we made a practice of injecting about 50 ml. more than we withdrew.

Subsequent Investigations.—In most cases the percentage exchange at the end of transfusion was estimated by differential agglutination. In 2 cases the rate of exchange also was determined from estimates made on serial samples during transfusion.

RESULTS

Blood Examinations

The direct Coombs test was invariably positive. Very weak positives were noted in 6 cases out of 58, and these infants were all very mildly affected. However, a strong positive test was not necessarily a sign of severity.

Hæmoglobin values in cord blood were below the normal range in more than half the infants (in our laboratory the hæmoglobin level of cord blood in normal infants usually lies between 98% and 124%, 100% being equivalent to 14·8 g. of hæmoglobin per 100 ml.). The mortality was higher in infants whose cord blood was anæmic. Samples taken a few hours after birth usually showed higher values, as expected. The difficulty of diagnosing anæmia in an infant a day old is just that of trying to decide whether an adult with a hæmoglobin level of about 100% is anæmic, having been told that he may or may not have had a transfusion of three pints of blood on the previous day. (For data on the transfer of blood from the placenta to the infant see DeMarsh et al. 1942.)

The concentration of bilirubin was less than 3 mg. per 100 ml. in the cord blood of all mildly affected infants (the normal range in our laboratory is 0·5–2·5 mg. per 100 ml.). Severely affected infants had values of over 4 mg. per 100 ml., the highest being 8·1 mg. per 100 ml.

The higher bilirubin values were found in the more anæmic infants. Bilirubin values sometimes rose very rapidly after birth, and comparisons were more difficult in later samples than in cord blood.

Erythroblastæmia was invariable in anæmic infants but inconstant in mildly affected cases.

Free Rh antibody was almost invariably present in the infant's plasma, but the amount was not well correlated with the other findings.

Clinical Results

The accompanying table shows that, of the 30 infants treated by exchange transfusion, 7 died and 23 recovered. The infants that died were 1 with frank hydrops fœtalis; 3 with severe anæmia whose condition at birth was critical and who died within 24 hours of birth; and 3 less severely affected who developed profound jaundice despite exchange transfusion and died 2–4 days after birth. Only one of the 23 survivors shows signs of damage to the central nervous system.

Among the survivors are a few infants whose condition was very critical at birth. The following are examples:

Case 1.—The mother had previously had 2 normal infants and an induced abortion. After the abortion she was transfused with three bottles of blood of unknown Rh type. This was followed by a severe hæmolytic reaction, and there is little doubt that she not only received Rh-positive blood but also was already at that time sensitised to Rh. The present infant was born 8 days before the expected date of delivery and was immediately seen to be pale and jaundiced; the spleen and liver were slightly enlarged. Blood examination 2 hours after birth showed red cells 1,150,000 per c.mm., Hb 35%, and bilirubin 11·6 mg. per 100 ml. A blood film showed that almost all the nucleated cells were erythroblasts or normoblasts, and there were 25% reticulocytes; the direct Coombs test was strongly positive. Exchange transfusion was carried out with Rh-negative blood, and at the end of the transfusion 90% of the cells in the infant's circulation were Rh-negative. However, the total hæmoglobin was only 57%, since ordinary diluted blood has been used, and a supplementary transfusion had to be given next day. The infant's subsequent progress was entirely satisfactory.

OUTCOME IN 63 CASES IN WHICH AN RH+ INFANT WAS BORN TO A MOTHER WHOSE SERUM CONTAINED RH ANTIBODY

Type of case	No. of cases	Treatment	No. of deaths		No. of recoveries	
			Within 24 hr.	At 48–96 hr.	Complete	With permanent damage to central nervous system
Stillbirth and hydrops fœtalis *	7	Exchange transfusion in 1 case	7	..	..	..
Infants with initial anæmia †	18	Exchange transfusion	3	3	12	..
Infants without initial anæmia	11	Exchange transfusion	..	..	10	1
	9	Simple transfusion	..	2	7	..
Infants first seen after first 24 hr. of life	4	Simple transfusion	..	..	3	1
Infants very mildly affected	14	No transfusion	..	..	14	..
Total	63	..	10	5	46	2

* 5 infants born dead; 1 with hydrops lived ½ hr.; another lived 5 hr. and was treated by exchange transfusion.
† Infants have only been included in this group if their hæmoglobin was less than 65% in cord blood or less than 80% in a venous sample taken within 24 hr. of birth.

Case 2.—The mother's first infant was normal, but she was then transfused with many bottles of blood of unknown Rh type. Her second infant died 4 or 5 days after birth, and it is recorded that it was very pale. In view of this previous history the mother's third pregnancy was terminated at 37 weeks. The infant was pale and a little jaundiced, and examination of its cord blood showed direct Coombs test positive, Hb 59%, and bilirubin 5·5 mg. per 100 ml. A blood film showed 20 nucleated red cells per 100 white cells. At 3¼ hours after birth the plasma-bilirubin level had risen to 9·3 mg. per 100 ml. An exchange transfusion was given, 470 ml. of blood being removed and 530 ml. of Rh-negative blood injected. By the 5th day of life the infant's bilirubin concentration had fallen to 2·8 mg. per 100 ml., and the infant was no longer jaundiced. The infant's hæmoglobin fell only very slowly after transfusion, and at 19 days of life it was still 86%; at this point no Rh-positive cells could be detected in the circulation. By the 47th day of life the hæmoglobin had fallen to 48%, but there were now some Rh-positive cells present. The infant's hæmoglobin thereafter rose spontaneously, and by the age of 78 days it had reached 70%. A few details are given in the following table:

Age	*Hb* (%)	*Bilirubin* (*mg. per 100 ml.*)	*Red cells* (*millions per c.mm.*)	*Rh-negative cells* (*millions per c.mm.*)
3 hours ..	76 ..	9·3 ..	3·0 ..	None
5 ,, ..	121 ..	7·0 ..	5·9 ..	5·9
5 days ..	108 ..	2·8 ..	— ..	—
19 ,, ..	86 ..	0·7 ..	4·5 ..	4·5
47 ,, ..	48 ..	— ..	— ..	—
60 ,, ..	58 ..	— ..	2·9 ..	1·6
78 ,, ..	70 ..	— ..	— ..	—

At 60 days there were only 1,600,000 Rh-negative cells per c.mm. in the infant's circulation, and it might at first appear that the elimination of these cells had significantly exceeded 1% a day. However, as Pickles (1947) has pointed out, allowance must be made for the infant's increasing body-weight. In the present case the infant had grown from 7 lb. at birth to 10½ lb. at the 60th day. Thus, to find the true survival-rate one must multiply 1·6 by 10·5÷7 and express this figure as a percentage of 5·9. The corrected survival is then 41%, which is very close to the expected figure.

Digitized by Google

Rate of Exchange

In the accompanying figure are plotted estimates of the numbers of Rh-positive and of Rh-negative cells in the circulation of an initially anæmic infant in samples taken at intervals during an exchange transfusion. The donor's blood had been artificially concentrated so that its count was 5,900,000 red cells per c.mm. The concentration of the infant's own (Rh-positive) erythrocytes fell from 1,650,000 per c.mm. to 560,000 per c.mm., whereas the count of Rh-negative cells rose rapidly to reach a concentration of 4,500,000 per c.mm. At the end of the exchange transfusion a further 40 ml. of Rh-negative blood was injected into the infant without withdrawing any more blood, and this raised the concentration of Rh-negative cells to 4,900,000 per c.mm.

So far we have emphasised the exchange of red cells but have not mentioned the exchange of plasma constituents, because we have been led to conclude that the removal of plasma constituents from the infant's circulation is unlikely to play any considerable part in the outcome. We have found that the amount of free Rh-antibody removed by exchange transfusion is less than would be expected if the infant's total amount of antibody were present in the plasma at the beginning of the transfusion. It seems that, as with other plasma-proteins, there is an equilibrium between the tissues and the plasma, and that removal of antibody from the plasma leads to the entry into the plasma from the tissues of a further amount so that a new equilibrium is reached at a slightly lower level. The lowering of plasma-bilirubin by exchange transfusion is even less, but here there is evidently the possibility of further production of bilirubin during the transfusion.

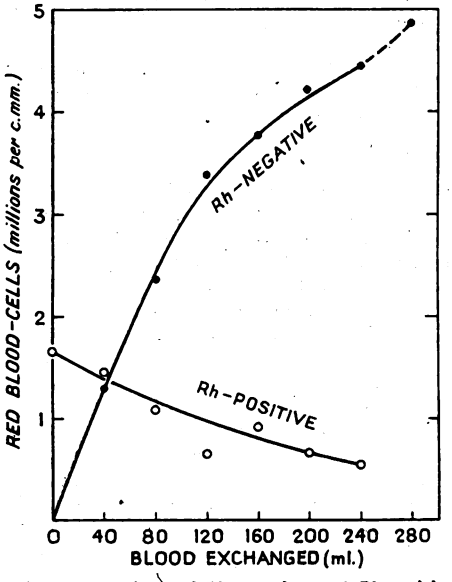
DISCUSSION

We must make it clear that we do not intend, on the basis of only 30 cases treated by this method, to try to demonstrate any effects on the morbidity and mortality of hæmolytic disease of the newborn. Cases of hæmolytic disease vary from being so severe as to kill the fœtus in utero at about the 24th week to being so mild as not to require any treatment. Moreover the severity depends on factors which cannot be assumed to operate to the same extent in different series. For example, there is the effect of a transfusion of Rh-positive blood given to a Rh-negative woman on the severity of hæmolytic disease in her subsequent offspring, which is well shown by our present series. Among our cases we found 48 affected infants born to mothers who had previously only given birth to healthy children; 16 of the mothers had, however, previously been transfused with blood of unknown Rh type, and 8 of their infants died. Among the remaining 32 infants born to mothers who had never been transfused there were only 2 deaths. The difference between these figures is highly significant. This finding is in agreement with the earlier observations of Diamond (1945) and Levine and Waller (1946).

Now, it is clear that, if one is seeing cases of hæmolytic disease in a district where, during the preceding few years, Rh typing has not been carried out before giving transfusions to women, one is likely to see more severe cases than if one practises in an area where few transfusions are given or where Rh tests have been made for many years. It is easy to think of other ways in which selection can lead to different kinds of cases being seen by different observers. For instance, in an obstetric unit one certainly sees more mild cases and probably more very severe cases than in a pædiatric unit; doubtless there are differences between places where families are large and those where families are small, for birth rank has some effect on severity. Also the reputation of a unit for treatment might foster the transfer of cases of greater than average severity to it. There is little doubt that, if two observers were each to collect cases in different parts of the country and to apply no treatment of any kind, a significant difference in mortality between the two series might be found. Moreover, it cannot even be assumed that the same observer sees a similar selection of cases in two successive years.

Apart from the above-mentioned factors one must consider the effect of better methods of diagnosis, with a resulting tendency to diagnose more mild cases. Thus at first sight it seems likely that the only way in which the value of exchange transfusion could be proved decisively would be by applying it to alternate cases in competition with, for example, simple transfusion. It might be possible to collect homogeneous groups —e.g., infants born to mothers previously transfused with Rh-positive blood, or, better still, infants with comparable changes in cord blood—and to treat alternate cases differently. Certainly it seems impossible to draw any conclusions from two different series unless one can be sure that the selection of the cases has been closely similar. It may not be necessary to attempt statistical proof if further evidence can be collected to show that the tissue damage in hæmolytic disease is in some way related to blood destruction, or if it can be shown that exchange transfusion is no more hazardous than simple transfusion and is more convenient. From the point of view of convenience it is most important that exchange transfusion should be carried out in such a way as to make it unlikely that the infant will need a further transfusion.

Since Rh-negative cells disappear from the infant's circulation at the rate of only 1% a day, and this rate is not influenced by the infant's total red-cell count, the main factor determining the subsequent course of events will be the concentration of Rh-negative cells in the infant's circulation at the end of the exchange transfusion. Now, it is evident that, however large a volume of blood is exchanged, provided that an equal amount of blood is injected and withdrawn, the final concentration of Rh-negative cells in the infant's circulation cannot exceed that of the donor's blood. Further,



Estimates of concentrations of Rh-negative and Rh-positive cells in samples taken from an infant during the course of an exchange transfusion: initial red-cell count of infant 1,650,000 per c.mm.; final count of Rh-positive cells 560,000 per c.mm.; red-cell count of donor's (Rh-negative) blood 5,900,000 per c.mm.; count of Rh-negative cells in infant's circulation after exchange of 240 ml. 4,480,000 per c.mm. Thus, after the exchange of an amount of blood about equal to the infant's blood volume, an 88% exchange was effected in this case. Finally (broken line), 40 ml. of Rh-negative blood was injected without further withdrawal to secure a final count of 4,910,000 Rh-negative cells per c.mm.

Digitized by Google

the count will only approach this level after a large exchange transfusion. Thus a count of 5,000,000 Rh-negative cells per c.mm. in the infant's circulation could be achieved either by using donor's blood with a count of about '6,000,000 per c.mm.' and carrying out an exchange of, say, 400 ml., or by using donor's blood with a count of only 5,000,000 per c.mm., carrying out an exchange of, say, 400 ml., and then injecting a supplement of, say, 50 ml. of donor's blood, without further withdrawal of blood from the infant.

It is clear that, though these are the factors which influence the concentration of Rh-negative cells in the infant's circulation at the end of transfusion, the concentration of Rh-positive cells remaining will depend on the infant's initial red-cell count and the volume of blood exchanged. Evidently the larger the volume exchanged the fewer will be the number of Rh-positive cells remaining.

Some of these effects are illustrated by the case reported above, where donor's blood with a red-cell count of 5,900,000 per c.mm. was used for an exchange transfusion in an infant with an initial red-cell count of 1,650,000 per c.mm. As an example, after the exchange of only 80 ml. of blood in this case, 65% of the cells in the infant's circulation were Rh-negative (see figure). According to a formula which only considers the exchange of blood in terms of volume (Wiener and Wexler 1946) this percentage exchange should only have been achieved after injecting and withdrawing an amount of blood equal to the infant's initial blood volume (probably a little over 200 ml. in this particular case).

Once an infant has been provided with a count of not less than 5,000,000 Rh-negative erythrocytes per c.mm., one can accurately predict the subsequent hæmoglobin levels by reckoning that 1% of the cells will disappear each day, and that the surviving cells will be diluted in a growing volume of plasma as the infant gains weight; an example has been given above. By the 30th day after transfusion the infant's hæmoglobin may have fallen to 60%, and it may subsequently fall a little lower. However, between the 30th and 60th days the infant's production of Rh-positive cells usually increases and no further fall in hæmoglobin occurs. Since the normal infant's hæmoglobin may fall to 70% between the 30th and 60th days values between 50% and 70% cannot be considered as very low, and it does not seem to be necessary to retransfuse infants at this stage unless the hæmoglobin falls below 50%.

Indications

The very mild course pursued by hæmolytic disease in all infants whose cord hæmoglobin was above 15 g. per 100 ml. and cord-bilirubin concentration below 3 mg. per 100 ml. and the stormy or fatal course pursued in infants whose cord blood showed anæmia or bilirubin values of over 4 mg. per 100 ml., has led us to conclude that the severity of a case of hæmolytic disease of the newborn can be assessed reliably from an examination of cord blood.

The value of examining cord blood for erythroblastæmia was stressed by Javert (1942), who also noted a slightly reduced hæmoglobin value and a considerably increased icteric index in a series of cases. Sadowski et al. (1947), who found bilirubin values between 4·9 and 8·1 mg. per 100 ml. in 3 severely affected infants, suggested that estimation of the cord bilirubin might be the best method of making an early diagnosis. Similarly, Pickles (1947) found plasma-bilirubin values between 3·0 and 7·5 mg. per 100 ml. in the cord blood of a series of affected infants.

We suggest that, if exchange transfusion is to be used as a method of treatment, it should only be carried out if the hæmoglobin of the cord blood is definitely below the normal range (say, below 14·5 g. per 100 ml.) or if the bilirubin value of the cord blood is above 4 mg. per 100 ml. (normal range, say, 0·5–2·5 mg. per 100 ml.). When the hæmoglobin is only just below 15 g. per 100 ml., or the bilirubin concentration is 3–4 mg. per 100 ml., it is useful to examine a blood film. A definite excess of nucleated red blood-cells (say, more than 10 per 100 white cells) should decide the issue in favour of an exchange transfusion. If cord blood has not been examined, the appearance of definite jaundice of the skin within 12 hours of birth in an infant whose blood gives a positive direct Coombs test is an indication for exchange transfusion.

SUMMARY

There are three grounds upon which exchange transfusion might be advocated for the treatment of cases of hæmolytic disease of the newborn:

(1) To raise the hæmoglobin level rapidly without increasing the blood volume. This might be of value in infants severely anæmic at birth, since we have found that these infants may have a raised venous pressure.

(2) To reduce to a minimum the amount of breakdown of Rh-positive cells during the critical first four days of life, since it is possible that the blood destruction in this phase is indirectly responsible for the tissue damage.

(3) To provide the infant with such a concentration of Rh-negative cells by a single operation that no further transfusions will be needed. In our experience this has proved to be a most substantial advantage, and we believe that, on this ground alone, exchange transfusion should receive widespread trial.

The percentage exchange effected by withdrawing the infant's own erythrocytes and replacing them by Rh-negative erythrocytes depends on the infant's initial red-cell count and the donor's red-cell count as well as on the total volume of blood exchanged. Thus, if the infant is anæmic and the donor plethoric, it will be easier to secure a good percentage exchange of red cells, and vice versa.

It is important not only to secure a good percentage exchange of Rh-negative for Rh-positive cells but also to leave the infant with a high absolute concentration of Rh-negative cells to tide it over the subsequent period, which may extend to 40 days or more, during which it is unable to maintain a satisfactory concentration of Rh-positive cells. This objective is best achieved by the use of donor's blood with a count of 5,000,000–6,000,000 erythrocytes per c.mm.

The severity of a case of hæmolytic disease of the newborn can be assessed reliably from an examination of cord blood; some criteria are given.

A favourable impression has been formed of the clinical effects of exchange transfusion, but the ability of this treatment to lower mortality and morbidity must still be considered unproved. Meanwhile, since we have not personally encountered any ill effects from it, we consider that it can justifiably be used as the most convenient method of treatment available. Nevertheless it is not a trivial procedure, and it should therefore be reserved for cases where a single transfusion of Rh-negative blood is not likely to suffice.

Most of the infants were treated in the obstetric department of the Postgraduate Medical School of London, but some were treated in Kingston Hospital, and a few of the earlier cases in St. Helier Hospital. We wish to thank the medical and nursing staffs of these departments for their help; Dr. L. K. Diamond, of Boston, for generous gifts of apparatus and for supplying us with information about his techniques at an early stage of his own work; the donors of the British Red Cross Society's Greater London Blood Transfusion Service; and the North and South London Blood Supply Depots for supplying Rh-negative blood at short notice.

References at foot of next page

Digitized by Google

INFLUENCE OF RESTRAINT ON AUTOMATIC MOVEMENTS

VALUE IN DIAGNOSIS

VLADIMIR VUJIC
M.D. Prague
PROFESSOR OF NEUROLOGY AND PSYCHIATRY

KOSTA KURTES
M.D. Belgrade
CLINICAL ASSISTANT, NEUROPSYCHIATRIC CLINIC

UNIVERSITY OF BELGRADE

THERE is a functional unity in the movements of all four limbs in quadrupeds and man. The fore limb (arm in man) of one side and the hind limb (leg in man) of the other side normally move simultaneously in the same direction during bodily progression.* This has been demonstrated also in reflexes obtained in decerebrate animals (Sherrington 1898). Arm-swinging is therefore an automatic accompaniment of walking; and Wilson (1928) observed in a case of largely right-sided parkinsonism that "the left arm was always advanced to a distinctly greater extent than usual, and this corresponded strictly to a slower advancement of the weak right leg."

Automatic arm-swinging in walking is often diminished or abolished in extrapyramidal lesions—e.g., parkinsonism, of which it is one of the earliest signs—but this also happens in severe spastic hemiparesis and in slight pyramidal lesions. According to Monrad-Krohn (1938) this movement is often absent in pyramidal and extrapyramidal lesions.

We have observed that healthy people walking while carrying something heavy in one hand swing the free arm more than when both arms are free; and that in a healthy person restraint of one arm increases the amplitude of swing of the other. In making this test it is essential to ensure that the restrained arm makes no movement whatever.

These observations led us to test arm-swinging in various pathological conditions, and we have found that, when a patient with predominantly unilateral parkinsonism walks carrying a book in his sound hand, or with that hand in his pocket or resting on his back, the automatic swinging of the unsound arm returns or is increased. When the sound arm is released, the swinging of the unsound arm is decreased or disappears. We have found the same thing in encephalitic pseudoneurasthenia, Sydenham's chorea, and hemichorea. (In some cases of masked encephalitis, and even in some cases of overt encephalitis if the patient can walk, some days may elapse before this phenomenon can be observed.) But in parkinsonism in which the unsound arm shows much hypertonus, in cerebral hemiparesis with spasticity, in unilateral pyramidal lesions without hypertonus, and in flaccid central paralysis of the arm, restraint of the sound arm does not bring back these movements in the unsound arm.

Reflexes may be linked so that inhibition of one calls forth the other reflex. For instance, swallowing and breathing are associated reflexes in that one of them must be inhibited to allow the other to act. Now, the inhibition of breathing—e.g., in a high wind—calls forth reflex swallowing. One would therefore expect that, in walking, restraint of one of the two limbs functionally associated as already described would stimulate reflexly the action of the other pair of limbs. This has been shown to be true of the arms and is probably true of the legs also, but this is difficult to prove.

Lescenko's Phenomenon

Other associated reflexes provide similar examples. Reflex blinking of one eye in normal people is strongly linked, and takes place simultaneously, with blinking of the other eye. But Lescenko has shown that if, in some cases of parkinsonism, while the patient fixes his gaze on an object, the demonstrator lowers one of the patient's upper eyelids and lifts that eyelid again, the uncontrolled upper eyelid of the other eye is automatically lowered; and, when the controlled eyelid is lowered again by the demonstrator, the uncontrolled eyelid is automatically raised.

It seems that, the normal lowering and raising of eyelids (blinking) being extremely rapid, the slower movement of the patient's eyelids by the demonstrator constitutes a form of restraint. Now, we have shown that restraint on one side causes active movement on the other. Further, the raising of the patient's eyelid by the demonstrator restrains its lowering; therefore such restraint provokes lowering of the opposite (uncontrolled) eyelid. In harmony with this finding is the fact that, in normal people, if the demonstrator prevents the subject from closing his eyes, attempts to blink are produced which are more frequent than normal.

Abduction of Legs

Raimiste (1909) has described how, in cerebral hemiplegia, restraint of active abduction of the sound leg elicits abduction of the unsound leg. According to Walshe (1921) "diverse forms of voluntary movements against resistance may, in certain cases of hemiplegia, always elicit the same response, whereas in other cases the form of the associated reactions could be completely modified according to the form of the voluntary movement of the sound arm." In these latter movements, to which Raimiste's phenomenon belongs, two facts are important according to Walshe: "(1) in most cases of residual hemiparesis there is considerable voluntary power in the affected leg; and (2) it is impossible in these circumstances, and even in the normal subject, to adduct or abduct the extended limb without also bringing into action with equal force the corresponding muscles of the crossed leg."

We do not agree with Walshe's first remark, because we have seen Raimiste's phenomenon even when the leg has been completely paralysed. His second remark, however, is evidence that there is a certain functional connexion between the legs in symmetrical abduction and adduction, probably stronger than in other symmetrical movements of the legs.

Pathological Movements

On the other hand, involuntary pathological movements—e.g., parkinsonian tremors—can be checked, in some cases by voluntary or other synergic movements. Even tonic muscular spasm which cannot be inhibited voluntarily may sometimes be overcome by synergic movements—e.g., voluntary blinking inhibits oculogyric lateral rotation (Golmann, quoted by Astwazaturow 1929). The automatic upward rotation of the eyeball on blinking inhibits lateral rotation.

*Exceptionally, in animals, both limbs of one side are advanced simultaneously, as in ambling.

DR. MOLLISON, MR. CUTBUSH: REFERENCES

DeMarsh, Q. B., Windle, W. F., Alt, H. L. (1942) *Amer. J. Dis. Child.* **63**, 1123.
Diamond, L. K. (1945) *New Engl. J. Med.* **232**, 447 and 475.
— (1947) *Proc. R. Soc. Med.* **40**, 546.
Howarth, S., Sharpey-Schafer, E. P. (1947) *Lancet*, i, 18.
Javert, C. T. (1942) *Amer. J. Obstet. Gynec.* **43**, 921.
Levine, P., Waller, R. K. (1946) *Blood*, **1**, 143.
Mollison, P. L. (1943) *Arch. Dis. Childh.* **18**, 161.
— Mourant, A. E., Race, R. R. (1948) *Med. Res. Coun. Memo.* no. 19. London.
Parsons, L. G. (1947) *Lancet*, i, 534.
Pickles, M. M. (1947) D.M. Thesis, Oxford University.
Ross, J. F., Finch, C. A., Peacock, W. C., Sammons, M. E. (1947) *J. clin. Invest.* **26**, 687.
Sadowski, A., Bromberg, Y. M., Brzezinski, A. (1947) *Nature, Lond.* **160**, 192.
Vaughan, V. C. (1946) *J. Pediat.* **29**, 462.
Wallerstein, H. (1946) *Science*, **103**, 583.
Wiener, A. S., Wexler, I. B. (1946) *J. Pediat.* **31**, 1016.
— — Shulman, A. (1948) *Amer. J. clin. Path.* **18**, 141.

Digitized by Google

DISCUSSION

If we consider the effect of restraint of the sound limb on automatic movement of the unsound limb, as already described, Raimiste's phenomenon, Walshe's second remark, and the fact that restraint of automatic arm-swinging on the sound side does not influence that on the unsound side in pyramidal lesions, we can conclude that restraint of either voluntary or automatic movements on the sound side elicits similar movements on the unsound side if those movements have been reduced or lost owing to a lesion of the motor tract (pyramidal or extrapyramidal) controlling those movements and when those movements are functionally connected.

Consequently the effect of such restraint is of diagnostic value where it is uncertain whether diminution or loss of movement is due to a pyramidal or to an extrapyramidal lesion. In pyramidal lesions, whether paresis of the arm is spastic or flaccid, restraint of the sound arm does not bring back the absent arm-swinging. Walshe (1921) found no sign of an associated reaction in arm or leg in flaccid paralysis, and concluded: "Some degree of hypertonus in a case of hemiplegia is an essential preliminary to the development of an associated reaction . . . the higher the degree of spasticity, the more forceful and the longer lasting will the associated reaction be."

In contrast to this, the absence of pronounced hypertonus in extrapyramidal lesions is a necessary condition to enable restraint of the limb on the sound side to bring back movements in the limb on the unsound side.

Most workers consider that the disappearance of arm-swinging represents a primary disturbance. There is no doubt that hypertonus also impedes these movements. Froment and Gardère (1921) consider that even in cases without evident hypertonus there is latent rigidity. Noica (1936) holds the same opinion and says that, where arm-swinging has been lost and yet hypertonus is not evident, hypertonus will develop later, at first only in walking and only in the proximal parts.

The fact that arm-swinging can disappear in unilateral pyramidal lesions with minimal paresis and no evident hypertonus might be regarded as supporting Wilson's (1928) opinion that arm-swinging is not purely automatic. But against this assumption is the observation that, in unilateral parkinsonism, deliberate swinging of the unsound arm inhibits arm-swinging by the sound arm. This harmonises with the fact that, in normal people, automatic movements are inhibited by attempts at voluntary control, and with our observation that, in unilateral parkinsonism, deliberately increased arm-swinging on the sound side does not affect arm-swinging on the unsound side.

These investigations cannot be regarded as complete. It would be especially interesting to study cases of post-concussional Mann's syndrome. In unilateral cerebellar lesions Wartenberg (1930), Marburg (1936), and Holmes (1946) find that arm-swinging disappears, whereas Grinker and Levy (1943) seem to think that it increases because of hypotonus. In a patient with a bilateral cerebellar lesion, more pronounced on the left side, we found that arm-swinging was diminished on the left side and that when the right arm was restrained arm-swinging increased in the left arm.

SUMMARY

Restraint of automatic arm-swinging on one side in normal people reinforces arm-swinging on the opposite side.

Restraint of arm-swinging on the sound side in unilateral extrapyramidal lesions—e.g., incipient parkinsonism, chorea minor, and encephalitic pseudo-neurasthenia—brings back the arm-swinging on the affected side if there is not much hypertonus.

In unilateral pyramidal lesions such restraint has no such effect, regardless of the state of muscular tone.

This test is of diagnostic value where it is doubtful whether loss of arm-swinging on one side is due to a pyramidal or to an extrapyramidal lesion.

REFERENCES

Astwazaturow, M. (1929) *Dtsch. Z. Nervenheilk.* **109**, 252.
Froment, J., Gardère, C. (1921) *Rev. neurol.* **37**, 1077.
Grinker, R. R., Levy, N. A. (1943) Neurology. Springfield, Ill.
Holmes, G. (1946) Introduction to Clinical Neurology. Edinburgh.
Marburg, O. (1936) in Bumke, O., Foerster, O. Handbuch der Neurologie. Berlin; vol. v.
Monrad-Krohn, G. H. (1938) Clinical Examination of the Nervous System. New York.
Noica, D. (1936) *Rev. neurol.* **65**, 812.
Raimiste, J. (1909) *Ibid*, **17**, 1366.
Sherrington, C. (1898) in Selected Writings of Sir Charles Sherrington. London, 1939.
Walshe, F. M. R. (1921) *Brain*, **46**, 1.
Wartenberg, R. (1930) *Neurol. Zbl.* **57**, 566.
Wilson, S. A. K. (1928) Modern Problems in Neurology. New York.

PRIMARY CARCINOMA OF THE LIVER

IN A BOY AGED 15

A. E. BEYNON
M.R.C.S.
MEDICAL DIRECTOR AND PHYSICIAN, CHEST RADIOGRAPHY CENTRE, NOTTINGHAM

THE ratio between primary and secondary carcinoma of the liver has been estimated as between 1 : 20 and 1 : 40. In 18,500 necropsies at Guy's Hospital (Hale White 1908) 24 cases (0·13%) of primary carcinoma of the liver were found, and the incidence in 6000 necropsies at the General Infirmary, Leeds (Stewart 1922) was the same. Data from several American and European hospitals revealed 144 cases (0·21%) in 65,501 necropsies, and reports collected from Asia and Africa give 416 cases (1·05%) in 39,701, and from a Singapore hospital 134 cases (0·76%) in 17,664 necropsies. Berman (1940) estimates that primary carcinoma of the liver is over forty times more frequent in some of the pigmented races than in the European.

The disease occurs mostly in or after middle age, and is said to be rare before 40 years of age. The earliest recorded case was in a baby girl aged 5 weeks (Langmead 1912). Berman (1940), in a series of cases in Bantu natives, found that 82·6% of the patients were 40 years of age or less, while the highest incidence was in the age-group 21–30. Steiner (1938), in a critical review of the literature, found 77 proved cases in children up to 16 years of age, 53% of them in children under the age of 2 years.

This disease is seen more often in men than in women; and of affected children Steiner (1938) observed that 68% were boys.

Symptoms.—There are no characteristic symptoms. Dull pain is a frequent feature and is referred to the liver region. Usually there are gastric upsets—i.e., anorexia, nausea, vomiting, diarrhœa, or constipation. Jaundice and ascites are uncommon. The average duration of life after the onset of symptoms is four months. No recovery has yet been reported. The incidence of symptoms in Berman's (1940) 42 cases was abdominal pain in 90%, asthenia in 86%, and dyspnœa, especially on exertion, in 26%; but this was a late symptom.

Physical Signs.—Most patients do not lose weight before admission to hospital but when bedridden lose weight rapidly. The liver is always enlarged and tender. Jaundice was noted in 43% and ascites in 55% of 34 cases (Berman 1940). Dilated superficial abdominal veins and œdema of the ankles and legs are found less commonly, and hæmatemesis rarely. Usually the temperature is either normal or subnormal, but some patients are febrile. The urine is unaffected in the early stages but later is diminished in amount and of high colour,

Digitized by Google

with an acid reaction. A trace of albumin may be found in cases with much ascites or œdema of the legs. The stools may become bulky, clay-coloured, and offensive.

Pathology.—Eggel (1901) found, in an analysis of a series of cases, that 68% were hepatomas and 32% arose from the bile-duct epithelium (cholangioma); whereas in Berman's (1941) series of 25 necropsies, 24 were hepatomas and 1 was a cholangioma, and in all cases microscopy showed cirrhosis of the liver.

Of Berman's series (1941) 57% had extrahepatic secondary deposits—in the lungs in 27 cases, and in the regional lymph-glands in 8. Metastases may be found in the ribs or the brain. Eggel (1901) reports that 66% had extrahepatic metastases, and that the spread may take place along the lymphatics to the glands in the hilum, the upper part of the abdomen, or the thorax, or via the blood-stream by direct extension into the portal and hepatic veins, giving rise to fresh growths in the liver or to secondary deposits in the lungs. The collected series of children included 52 cases of hepatoma, and 3 of cholangioma, 22 being unclassified. In 27% of these cases there were extrahepatic secondary deposits.

Treatment is purely palliative.

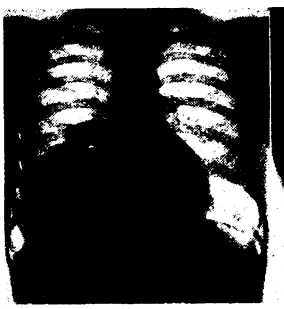


Fig. 1—Postero-anterior view (April 2, 1946) showing large round mass in lower lobe of right lung.

Fig. 2—Right lateral view (April 2, 1946) showing two rounded tumours situated anteriorly in lower lobe of right lung.

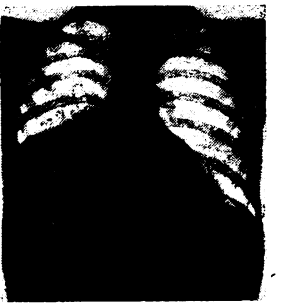


Fig. 3—Postero-anterior view (April 30, 1947) showing increase in size of tumour in lower lobe of right lung. Rest of lung field remains clear. Diaphragm is raised owing to enlargement of liver.

CASE-RECORD

A boy, aged 15, born on June 4, 1930, volunteered with his school group for mass miniature radiography in March, 1946, and was recalled for a large film of his chest and for further clinical examination. I first saw him on April 11, 1946, when he was completely symptomless but admitted to a dull pain in the epigastrium six months earlier, which had lasted a fortnight and had not recurred. His weight was stationary. He gave a past history of "influenza" in December, 1945, but had recovered quickly from this.

On examination.—He was thin but not anæmic. No enlarged glands could be detected in neck, axillæ, or groins. Liver enlarged two fingerbreadths below costal margin; spleen not palpable. A localised swelling in epigastric region moved with the liver on respiration; it was hard and craggy, with an irregular and nodular surface. It was not cystic and did not pulsate. Chest: grossly diminished breath sounds, with diminished vocal resonance over right lower lobe, anteriorly and posteriorly; no adventitious sounds.

Physical signs of liver tumour suggested malignancy and the patient was admitted to hospital.

Investigations (April, 1946).—Erythrocyte-sedimentation rate (E.S.R.) (Westergren) 126 mm. in 1 hour. Wassermann reaction negative. Blood-count: red cells 5,181,000 per c.mm.; Hb 92%; colour-index 0·9; white cells 4400 per c.mm. (polymorphs 60%, large lymphocytes 8%, small lymphocytes 23%, large mononuclears 4%, eosinophils 5%). Radiography of chest (April 2, 1946) showed two large rounded and clearly defined tumours in the anterior part of the lower lobe of the right lung, suggesting hydatid cysts (figs. 1 and 2). Rest of lung fields clear, with no evidence of disease.

Admitted to the Brompton Hospital on July 10, 1946, he was febrile (temperature 100°F) and pale, with female facies and gynæcomastia. There was a large slightly tender mass, moving with respiration, in the epigastrium, and the liver was much enlarged. Testes small; female distribution of pubic hair. Poor air entry at right base of chest.

Investigations (July, 1946).—E.S.R. 140 mm. in 1 hour. Blood-count: slight hypochromic anæmia and a lymphocytosis of 37%; Casoni test and Friedman test negative; bleeding and clotting times normal, and no abnormality in sputum. Radiography "showed an opacity in the right lower zone situated anteriorly and also a rounded tumour in the abdomen. It was suggested that, if the opacity in the chest was intrapulmonary, hydatid disease should be considered, but primary mediastinal teratoma is the most likely diagnosis." (L. G. B.)

Diagnostic pneumoperitoneum suggested that the epigastric mass was connected with the liver but not with the mass in the lower zone of the chest on the right side.

Aspiration biopsy of the mass in the abdomen produced tissue characteristic of primary carcinoma of the liver (hepatoma). Section was composed mainly of blood-clot. Tumour cells showed very considerable irregularity in shape and size and were closely packed together; some of them were binucleated.

Patient was referred for deep X-ray therapy, but this was ineffective and was therefore discontinued. He was discharged on Aug. 15, 1946, and the prognosis was considered hopeless.

Progress.—He remained symptomless and enjoyed good health but did not return to school. He spent a great deal of time motor-cycling and was leading an active life out of doors. His weight slowly increased, from 6st. $7^1/_4$ lb. on Oct. 31, 1946, to 6st. $10^1/_2$ lb. on April 30, 1947.

In October, 1946, he had a short sharp attack of pleurisy on the right side, but quickly recovered. In November he was brighter and active, but had no symptoms apart from a recent gastric upset with vomiting and diarrhœa, and loss of $2^1/_2$ lb. in 3 or 4 weeks. This weight was regained and at Christmas he felt very well, and was motor-cycling. At the end of April, 1947, however, he was much weaker, with anorexia and attacks of nausea and vomiting about once a week. He was now thin and apathetic, with no interest in his surroundings. He moved with difficulty, and it required great effort on his part to get on to the examination couch. The liver now almost filled abdomen, and the tumour in the epigastrium was larger and possibly slightly tender. A small amount of ascites was probably present.

Investigations (May 5, 1947).—van den Bergh and Fouchet's reactions negative. Blood-count: red cells 4,340,000 per c.mm.; Hb 68%; colour-index 0·79; hæmatocrit 34%; mean corpuscular volume 79·0 c.μ.; mean corpuscular Hb concentration 29·0%; E.S.R. (Wintrobe) 3 mm.; white cells 8200 per c.mm. (polymorphs 70%, lymphocytes 20%, large monocytes 9%)—a normocytic hypochromic anæmia.

The low E.S.R. is rather misleading in view of the malignant condition. Next day the E.S.R. was repeated by the Westergren method and was 120 mm. in the first hour.

Radiography of chest (April 30, 1947) showed that the secondary growths had not increased much (fig. 3).

The boy died on July 5, 1947, almost sixteen months after his first X-ray examination. Necropsy was refused.

COMMENT

There are several interesting features in this case: (1) The striking lack of development of male sex characteristics. (2) The misleading maintenance of body-weight, probably because the increase in size and weight of the liver balanced the obvious loss of flesh. (3) The long period before the development of symptoms, in spite of the two large secondary deposits in the lung. The first and single gastric upset appeared in November, 1946, seven months after his first clinical examination. It was not until April 28, 1947, a year after he was first seen, that he had regular attacks of nausea and vomiting at weekly intervals, and he died about two months later. (4) Comparison of the X-ray film of April, 1946, with that of April, 1947, shows that the two large secondary deposits had increased but slightly during the year.

Digitized by Google

(5) The absence of icterus throughout, both clinically and by van den Bergh reaction.

SUMMARY

A case is reported of primary carcinoma of the liver detected in a schoolboy aged 15 by a mass miniature radiography unit.

Radiography showed two clearly defined tumours in the lower lobe of the right lung. The rest of the lung fields was clear. An apparently malignant tumour of the liver was found on clinical examination. Aspiration biopsy confirmed the diagnosis.

The boy led a normal symptomless life for about a year, but then his condition rapidly deteriorated, and he died about sixteen months after the original radiography. There was no jaundice, and the metastases in the lung increased but slightly.

I wish to thank Dr. T. H. Gillison, of Ilkeston, Derbyshire, for his keen coöperation and the case-record; Dr. W. D. Brooks for allowing me to quote the findings while the boy was under his care in the Brompton Hospital; and Dr. L. G. Blair for the radiological reports.

REFERENCES

Berman, C. (1940) *S. Afr. J. med. Sci.* **5**, 54.
— (1941) *Ibid*, **6**, 11.
Eggel, H. (1901) *Beitr. path. Anat.* **30**, 506.
Langmead, F. S. (1912) *Proc. R. Soc. Med.* **6**, section Children, 46.
Steiner, M. M. (1938) *Amer. J. Dis. Child.* **55**, 807.
Stewart, M. J. (1922) see *Brit. med. J.* ii, 1065.
White, W. H. (1908) in Allbutt and Rolleston's System of Medicine, vol. IV, 215.

DELAYED PNEUMONITIS IN A BERYLLIUM WORKER

REPORT OF A CASE

JOHN N. AGATE
M.A., M.B. Camb., M.R.C.P.
From the Department for Research in Industrial Medicine (Medical Research Council), the London Hospital

RECENT reports from the United States show that the handling of beryllium compounds is attended by a risk of dermatitis or of respiratory disease. This had already been discovered by Weber and Englehardt (1933) in Germany; and Gelman (1936) in Russia, and Marradi Fabroni (1935), experimenting with animals, had suggested calling the lung disease "berylliosis," but no reports appear to have come from Europe since 1943. American writers have lately helped to clarify the clinical picture, and to some extent the pathology, of these diseases as they affect man. Nevertheless, some of the ætiological factors have still to be discovered.

In the 'twenties and early 'thirties negligible quantities of beryllium compounds were used in the United States, but during and since the late war the consumption has risen steadily, and with it the incidence of these occupational diseases. Two of the principal industries now concerned are those in which fluorescent lamps and copper alloys are made. To supply them, several factories have been engaged in extracting beryllium from ore, and it was here that the hazards were first encountered.

In Great Britain the use of beryllium has lagged somewhat behind, especially in war-time, for reasons of expediency. A few of the compounds, however, have been used experimentally here from about 1936 onwards. Developments in the British fluorescent lamp industry have been rapid of late, and the commercial use of the phosphorescent powders which contain beryllium has already begun. The more this element is used in this country, the more likely are we to have to share the American experiences of its toxicity.

Van Ordstrand et al. (1943) described "chemical pneumonia" in 3 men extracting beryllium oxide from ore. The disease came on soon after exposure, was acute, and was characterised by cough, mild pyrexia, and dyspnœa. Van Ordstrand et al. (1945) reported 38 similar cases and 90 others of nasopharyngitis and tracheobronchitis; most of these came from the same industry, but in some there had been exposure to dust and fumes in the preparation of pure beryllium metal and the making of beryllium-copper alloys. There were 5 deaths.

Hardy and Tabershaw (1946) described, as a separate clinical entity, "delayed chemical pneumonitis." The occurrence of 17 such cases in one fluorescent-lamp factory in Salem, Massachusetts, suggested that the phosphorescent powders used there were to blame; the one chiefly handled was a mixed silicate of zinc, beryllium, and manganese. There were 6 deaths in this important series, and several survivors were left seriously incapacitated. Pascucci (1948), in a later follow-up, which also included 15 fresh cases, reports that 30% of the patients have died and 30% are still unimproved. The remarkable feature was the delay between exposure to risk and the appearance of symptoms. In one instance the interval was three years. Wilson (1948) states that the delay may be as long as six years.

In September, 1947, an exchange of information at the Sixth Saranac Symposium of the Edward L. Trudeau Foundation, Saranac Lake, N.Y., indicated that scarcely any of the beryllium compounds in use in industry could be handled with absolute safety. The soluble salts, such as sulphate, fluoride, and oxyfluoride, had already been held responsible for the dermatitis and for much of the acute respiratory disease (Gelman 1936 and other workers). But fresh evidence now suggested that cases of both acute and delayed respiratory disease had resulted from working with beryllium compounds, soluble or insoluble, in most of the industries concerned. Thus, most but not all of the acute cases had come from factories where beryllium oxide was extracted from ore, whereas most but not all of the delayed cases had come from the lamp industry. Recent or past exposure to beryllium compounds was the one factor common to all the many cases then under discussion. There was also reason to think that certain people were unusually susceptible, for "neighbourhood cases" were described, in which the victims could only have been exposed to very slight risk, because they lived close to factories yet had never been inside them. The diagnosis in one at least of such cases was supported by necropsy findings.

Gardner (1946) had already estimated that the number of authentic cases of delayed pneumonitis was 60, and he referred to typical cases from the radio-valve and neon-sign industries besides those already mentioned.

Stimulated by these accounts and by the lack of similar reports from the United Kingdom, I began to make inquiries in some British factories, and was soon told of a man who had once worked with beryllium compounds and who was now said to be seriously incapacitated by "sarcoid." Further investigation suggested that his case was one of delayed pneumonitis as just described; it may be the first to have occurred in Great Britain.

CASE-RECORD

A physicist, aged 36, was engaged in research on filament and mercury-vapour lamps from his graduation in 1936 until 1941. He was slightly exposed to dust between 1938 and 1941, when he was filling some 200 lamps with powdered sulphides of zinc and cadmium. He noted no ill effects from this. Between December, 1941, and December, 1942, he worked on the development of tubular fluorescent lamps. He handled about 500 tubes, which had already been coated internally with the phosphorescent powders containing zinc beryllium manganese silicate and magnesium tungstate. He had to clean the last 3 inches of each tube with a duster; from time to time he shook out the duster and a cloud of dust arose. The next stage—the sealing-in of electrodes and exhaustion of the tube—was not without risk, because he sometimes had to suck at a side tube, and could have inhaled powder. He was working in a small laboratory, but the coating processes were all done in a separate room. During October and November, 1942, small quantities of these phosphor

Digitized by Google

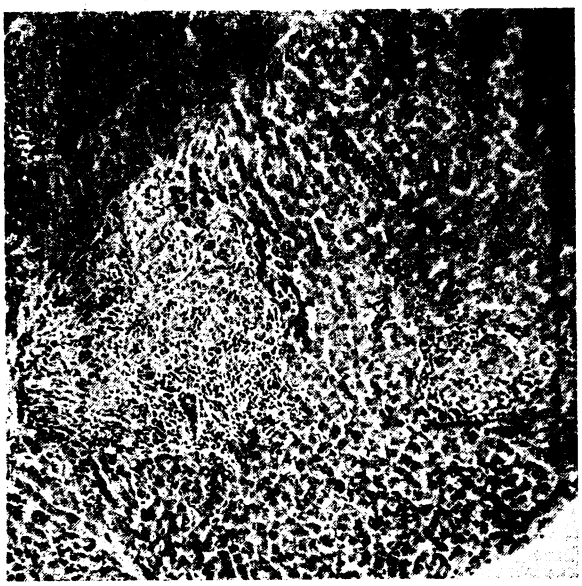


Fig. 1—Liver-biopsy specimen showing focal granulomatous lesions. (× 95.)

powders containing beryllium were prepared, ground, and heated in his laboratory, only a few feet from his bench. This undoubtedly increased the risk to which he was exposed. After December, 1942, his contact with phosphors was negligible; for the next two years he worked in other rooms and only occasionally chanced to walk through the laboratory.

In November, 1945, three years after his last significant exposure, he had a feverish cold, and a dry cough developed when he returned to work three days later. After another month the cough became productive, yielding a little yellow-green sputum, and he began to be dyspnœic on exertion; he could neither run for a bus nor climb a hill. At the same time he began to lose weight rapidly, and by February, 1946, was already 23 lb. below normal. Radiography of his chest then led to a tentative diagnosis of miliary tuberculosis. He could walk only about 30 yards on the level. He was admitted to hospital, where miliary tuberculosis was excluded and pulmonary sarcoidosis diagnosed. All of many sputum examinations were negative for tubercle bacilli; a Mantoux test at 1 : 1000 dilution was positive; and a blood-count showed 6,000,000 red cells per c.mm. and Hb 130%. The patient continued to be seen at various hospitals for a year and a half after his discharge. During this time his weight was still falling, his appetite was poor, and he had to be absent from work repeatedly because of attacks resembling acute bronchitis. His chief symptom, which varied in severity, was always dyspnœa on exertion and at rest.

On examination in February, 1948, I found that he weighed only 7 st. 5 lb., having lost 51 lb. in all. He was dyspnœic at rest and slightly cyanosed, but there was no clubbing of his fingers. The cardiovascular system was normal except for an accentuated second heart sound in the pulmonary area. The chest expansion was only 1 in. The percussion note of the chest was resonant, but multiple rhonchi and coarse crepitations could be heard in all areas. The liver edge was palpable $1^1/_2$ in. below the costal margin, but the upper limit of hepatic dullness in the chest was displaced downwards. The spleen was not palpable, and only one small lymph-gland was felt in the neck. No glands were discovered elsewhere, and the parotids and uveal tracts were normal.

He was again admitted to hospital. During a stay of three weeks there was no fever, but the respiratory-rate at rest varied remarkably, between 18 and 38 per min. On the slightest exertion he was dyspnœic to the point of distress.

Vital capacity: 1470 c.cm. A healthy man of this patient's height and weight might have had a vital capacity of 3800 c.cm., calculated from surface area by the formula of West (1920). The capacity recorded was only 39% of this.

Sputum: repeatedly negative for *Myco. tuberculosis*.

Erythrocyte-sedimentation rate: 7–13 mm./1 hour (Wintrobe).

Mantoux test: 1/10,000 negative and 1/1000 negative.

Blood-count: Hb 112%, red cells 6,412,000 per c.mm., white cells 5300 per c.mm. (polymorphs 44%, eosinophils 1%, lymphocytes 45%, large hyaline cells 10%).

Electrocardiogram: some right ventricular preponderance.

Circulation-time: arm to breath (ether min. 5) = 7–9 sec., arm to face (histamine phosphate 0·1 mg.) = 25–28 sec.

Glucose-tolerance test: within normal limits.

Liver-function tests: van den Bergh, indirect reaction 0·5 mg. bilirubin per 100 ml. Alkaline phosphatase, 6 units. Thymol turbidity, 6 units. Cephalin cholesterol flocculation, 1. Serum colloidal gold, 0.

Plasma-proteins: total 6·6 g. per 100 ml. (albumin 4·4 g. and globulin 2·2 g. per 100 ml.)

Beryllium in urine (spectrographic technique): on admission, nil detected. After a course of dimercaprol (BAL), nil detected.

Radiography: X-ray films of the patient's hands and feet in April, 1946, and April, 1948, showed no abnormality.

Radiography of his chest four months after the onset of his illness showed a fine punctate or granular marking scattered throughout both lung fields, the lesions being 0·5–1·0 mm. across. The cardiac outline was normal. Eight months after the onset there was a similar uniform fine punctate marking, with some evidence of a reticular pattern. Seventeen months after the onset there was more definite appearance of reticulation in all areas with some small scattered nodules, 2 mm. across, at the periphery of the mid-zones. The right interlobar septum had been drawn upwards. There was broadening of the upper half of the cardiac shadow, especially in the region of the pulmonary artery: the hilar vessels were prominent. Twenty-one months after the onset more definite fine nodulation was apparent in the upper mid-zones, though the other appearances were unchanged. Thirty months after the onset there was some clearing of the lower zones, where the appearances suggested emphysema. In the upper and mid zones there was a coarse reticular pattern with much increase of linear striæ, suggesting fibrosis; nodulation was less in evidence. The diaphragm was flattened in the shape of a cone, the mediastinal shadow was broad, and the hilar vessels were very prominent. There was no enlargement of the left auricle on screening in the oblique positions with barium emulsion in the œsophagus.

Drill biopsy of liver showed focal granulomatous areas scattered throughout the tissue. These areas consisted mainly of macrophages and small round cells, with a few fibroblasts and occasional epithelioid cells, but no giant cells. There was no necrosis or fibrosis. The surrounding liver parenchyma was normal (figs. 1 and 2).

Ultraviolet microscopy showed aggregates of sharply defined spiculate particles with a bright white fluorescence in the middle of some of the granulomatous lesions. These were seen only in the abnormal tissue. In specimens of normal liver obtained from necropsies and examined by this method,

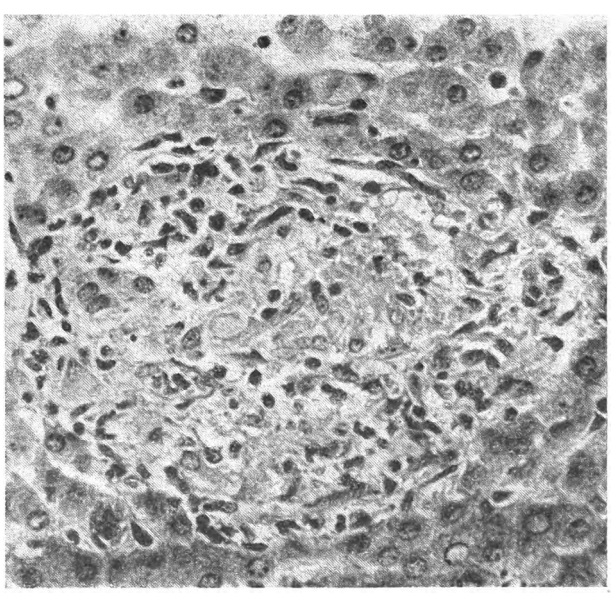


Fig. 2—The smaller of the two granulomatous lesions shown in fig. 1. (× 450.)

Digitized by Google

single fluorescent bodies were sometimes seen in the sinusoids and small aggregates in the region of the portal vein, but these bodies were rounded and often had a yellowish tint. Possibly the particles within the lesions in the present case consisted of the original fluorescent powder, but the test cannot yet be considered conclusive.

Progress.—The patient has not improved at all since his admission to hospital. He is remarkably dyspnœic, can do light laboratory work, but is often absent as a result of minor respiratory infections which drive him to bed.

CLINICAL PICTURE

Hardy and Tabershaw (1946) originally reported 17 cases from one factory. Since then, others have occurred there, and men and women engaged in all the stages of fluorescent lamp making have been affected. The original 17 were variously exposed to zinc beryllium manganese silicate for from 5 months to 5 years. The present patient was exposed to just the same risk for a year, and there was a delay of 3 years before his first symptoms appeared; this is also in keeping with the other cases. Hardy and Tabershaw observed that loss of weight at the onset, dyspnœa on exertion, cough, and fatigability were present in nearly all their patients. They wrote of weight losses of 20, 34, and even 40 lb. within the first year of illness. Adventitious sounds were heard in the chest in 13 of their cases, tachycardia was present in 10, and an accentuated pulmonary second sound in 6, and an abnormally high resting respiratory-rate was found in 10 out of the 11 cases in which it was recorded. The liver was enlarged in 2 cases, and the spleen in 2. In only 2 patients could adenopathy be found, and in 2 there were skin lesions which later proved to be granulomatous. The clinical findings in the present case agree very closely. Though anorexia was not an outstanding symptom, weight loss, dyspnœa, and cough were; indeed, the patient had lost 23 lb. in the first three months, and 51 lb. within 2 years. He had no generalised adenopathy and no splenomegaly, but the edge of his liver was palpable, and a biopsy specimen contained granulomatous lesions. Hardy and Tabershaw refer to one necropsy in which granulomatous tissue was found in the liver, lungs, and hilar glands, and Hardy (personal communication 1947) found similar granulomata in liver-biopsy material from a later case.

The radiographical appearances in Hardy and Tabershaw's series of cases were described (by Wilson and Sosman) as being in three stages: (1) "granularity," (2) a superimposed reticular pattern, and (3) nodulation. The appearances in the present case do not correspond exactly to these stages; for, though there are signs of "granularity" and reticulation, the nodular stage is less pronounced than in some of the original films which I have seen. However, Wilson (1948) now allows that not all cases progress in the three stages originally described, and he adds a further stage of coalescence of lesions in the upper zones, with emphysema at the bases, just as was seen in the later films in the present case.

The chronicity of the disease in this case, and the serious residual disability, are typical of many. In short, there appears to be a sufficient resemblance between this case history and those of others who had delayed chemical pneumonitis to justify making the same diagnosis. Consequently, the disease must be attributed to the patient's former occupation.

DIAGNOSIS

The present case was first tentatively diagnosed as one of acute miliary tuberculosis on radiological grounds; later it was called Boeck's sarcoidosis. This is of interest because these diagnoses were made at first in the earliest American cases. Indeed it was only when a number of alleged cases of "sarcoidosis" occurred together in one factory that this diagnosis was questioned and an occupational ætiology suspected.

Miliary tuberculosis may be excluded by the absence of the typical pyrexia or other evidences of a gross infective process, and eventually on the course of the disease. The resemblance to Boeck's sarcoidosis, however, is undeniable, and a differential diagnosis may not be easy to make, particularly since both diseases produce granulomatous hepatic lesions. Schaumann (1936), Nickerson (1937), van Buchem (1946), and others have described these lesions in necropsy material from cases of sarcoidosis, and Scadding and Sherlock (1948) have found them in biopsy specimens. In the present case the radiographical appearances also could have been taken for those of pulmonary sarcoidosis, though in the latter disease there is usually a contrast between the mild subjective symptoms and the grossly abnormal X-ray findings (Reisner 1944). Moreover, in the present case there were no skin or ocular lesions, no adenopathy, and no abnormalities of salivary glands or of fingers; the loss of weight was remarkably severe, and there were weakness, tachypnœa, and a residual disability far greater than would be expected in sarcoidosis. These clinical features therefore make the latter diagnosis unlikely, and a positive Mantoux reaction in 1946 and normal radiograms of the extremities are further evidence against it.

Finally, there is the histology of the granulomata in the liver, in which there is pleomorphism and the cells consist mainly of macrophages and fibroblasts, with considerable round-cell infiltration but no giant cells. In the lesions of sarcoidosis it is usually reported that the cells are mostly epithelioid cells, with giant cells, but with less round-cell infiltration.

The other differential diagnoses to be considered were generalised carcinomatosis, the pulmonary mycoses, and the pneumonoconioses. The last-named could be excluded by the occupational history. The acute pneumonitis of beryllium workers, too, is differentiated by the mode of its onset, which is never much delayed, and by the fact that it usually resolves satisfactorily if the patient is given rest and removed from exposure. Valvular heart disease with failure may be suggested by the cyanosis, dyspnœa, and radiographical appearance of the heart, but in the present case the other typical signs were absent.

The urine of this patient contained no beryllium, even when tested by the most sensitive method known. Since, however, more than 5 years had elapsed since his chief exposure, it is reasonable to assume that any beryllium not fixed in the tissues would have been excreted long before. The total absorption is unlikely to have exceeded a few milligrammes.

This disease always presents clinically as one which affects the lungs, but granulomata have also been detected in liver, glands, and skin; hence the pulmonary lesions appear to be only part of a more generalised pathological condition. Experiments on animals may eventually explain the process involved. It is of interest to speculate whether beryllium compounds elicit this response by direct action or by sensitising the tissues to some other agent. In some respects lung diseases due to beryllium resemble infections. On the other hand, Grier et al. (1948) have described granulomata in the skin after cuts from broken fluorescent lamps; these granulomata contained epithelioid cells and giant cells, and in one case beryllium was detected in excised tissue.

SUMMARY AND CONCLUSIONS

A laboratory worker developed a chronic pneumonitis three years after exposure to a phosphorescent powder (zinc beryllium manganese silicate) used in making fluorescent lamps. The patient inadvertently exposed himself to risk, for it is not generally understood that

Digitized by Google

the degree of exposure needed for this dust to cause harm is much less than that usually needed to bring about occupational pulmonary disease. Cough, dyspnœa, and extreme loss of weight were the chief clinical features. Radiography revealed extensive bilateral pulmonary disease. Granulomatous lesions were found in the liver without biochemical evidence of liver disorder.

The commercial use of beryllium has expanded so much in the last three years that further cases may be expected in Great Britain. If the onset of the disease can be delayed as long as six years, the ætiology may not be suspected unless an adequate history is taken of the patient's occupations.

Where possible, substitution of other compounds in place of those of beryllium is clearly the best preventive measure. In processes where this element must still be used, vigorous suppression of all dust and fumes, and regular medical supervision of workers are necessary. The prognosis of this disease is poor and treatment ineffectual; the disability that is left, as in the present case, may be serious and permanent. Legislation to provide for compensation might perhaps be considered even before the occurrence of any extensive outbreak of cases in Great Britain.

I wish to thank Dr. Donald Hunter, director of the Department for Research in Industrial Medicine, for his encouragement and advice; Mr. Frank Ellis for performing the liver biopsy; Dr. James Maxwell for allowing me access to the patient and his earlier radiograms; Dr. P. L. Bidstrup and Miss J. Garrad for their assistance; the staff of the Bernhard Baron Institute of Pathology, London Hospital, for their help; and Mr. G. Smailes and Mr. F. V. Welch, of the National Institute for Medical Research, for the photomicrographs.

REFERENCES

Gardner, L. U. (1946) Transactions of the 11th Annual Meeting of the Industrial Hygiene Foundation of America.
Gelman, I. (1936) *J. industr. Hyg.* **18**, 371.
Grier, R. S., Nash, P., Freiman, D. G. (1948) *Ibid*, **30**, 228.
Hardy, H. L., Tabershaw, I. R. (1946) *Ibid*, **28**, 197.
Marradi Fabroni, S. (1935) *Med. Lavoro*, **26**, 297.
Nickerson, D. A. (1937) *Arch. Path.* **24**, 19.
Pascucci, L. M. (1948) *Radiology*, **50**, 23.
Reisner, D. (1944) *Amer. Rev. Tuberc.* **49**, 289.
Scadding, J. G., Sherlock, S. (1948) *Thorax*, **3**, 79.
Schaumann, J. (1936) *Brit. J. Derm.* **48**, 399.
van Buchem, F. S. P. (1946) *Acta med. scand.* **124**, 168.
Van Ordstrand, H. S., Hughes, R., Carmody, M. G. (1943) *Cleveland Clin. Quart.* **10**, 10.
— — De Nardi, J. M., Carmody, M. G. (1945) *J. Amer. med. Ass.* **129**, 1084.
Weber, H. H., Englehardt, W. E. (1933) *Zbl. GewHyg.* **10**, 41.
West, H. F. (1920) *Arch. intern. Med.* **25**, 306.
Wilson, S. A. (1948) *Radiology*, **50**, 770.

"... Many thousands of hours of the time of the school medical officers and nurses have been lost due to our failure to take the family as the unit. In all our work the golden rule would be to do what is best for the family, for instance, in the question whether the child should attend a nursery school should be judged on its merits—in some cases the family life would be benefited by a child attending, in others quite the reverse. The pros and cons must be measured for the individual child and family. With the exception of those parents with diseased minds who are deliberately cruel; at almost any cost, the family should be kept together. ... We must intensify our efforts to help the problem families in their own homes, as is done by the Family Service Units. We must teach the mother—this does not necessarily mean lecturing her—we must help her by showing how she could manage better in her (perhaps) poor home, use the existing kitchen range and the defective tools with which she has to do her jobs; or perhaps she may need help and rest which a rehabilitation centre, such as Brentwood, can give, where she may take her children and where she will be taught homecraft in the right way, by the right people, and be made ready to make a fresh start. Our aim must be to 'capture the mother'—to use the greatest force in the world, mother love. If we teach the mother rightly she will do the job of teaching the children for us, and we must remember that the teaching she gives goes on all the time." —Dr. J. L. BURN, *J. R. Inst. publ. Hlth*, October, 1947.

Reviews of Books

Treatment of Heart Disease

WILLIAM A. BRAMS, M.S., M.D., PH.D., associate professor of medicine, Northwestern University, Chicago. London: W. B. Saunders. 1948. Pp. 195. 17*s*. 6*d*.

WRITING as a practical clinician, and basing his work upon his own experience, Professor Brams has produced an excellent textbook. Dogmatic without being intolerant, comprehensive yet never diffuse, he gives the medical student and the general practitioner the information they need for dealing with patients with heart disease. One of his great merits is that, unlike many writers of textbooks on therapeutics, he has restricted himself to his subject and avoided unnecessary discussions of clinical and diagnostic problems. A long first chapter on the "pharmacologic action of drugs used in the treatment of heart disease," saves much unnecessary repetition in the sections dealing with individual disorders.

Major Endocrine Disorders

(2nd ed.) S. LEONARD SIMPSON, M.A., M.D., F.R.C.P., physician, Willesden General Hospital. London: Oxford University Press. 1948. Pp. 552. 42*s*.

THIS is not a textbook of endocrinology: and indeed there is no reason why it should be, except that no British author has yet attempted to write one, which is perhaps a pity. Since he is not writing a textbook, Dr. Simpson is under no obligation to give a carefully balanced account of the subject, with much space for the common or important aspects, and little for rarities, museum pieces, or details of tests performed in this country by perhaps no more than a score of specially trained experts. Instead he treats the specialty from the personal point of view, emphasising aspects in which he is specially interested, such as the adrenal cortex. Other aspects—such as recent work on the œstrogens—in which he has no particular interest are treated summarily and with less care for accuracy. It is as though he had set himself to clarify his own views by putting down the product of his own clinical experience and of his wide reading of the literature. Unless the reader appreciates this personal approach he may be slightly irritated by the frequent use of the first person singular. The autobiographical exposition, however, has advantages as well as disadvantages. Dr. Simpson has taken an active interest in endocrinology for many years, and this account of his experience represents very fairly the views of an enlightened physician who keeps abreast of recent advances in the subject. Though it is a second edition, the book has been virtually rewritten and is now at least four times as big as it was in 1938. There are many excellent illustrations and the standard of production is high.

Surgical Treatment of the Abdomen

Editors: FREDERICK W. BANCROFT, M.D., F.A.C.S., professor of clinical surgery, New York Medical College; PRESTON A. WADE, M.D., F.A.C.S., associate professor of clinical surgery, Cornell University. Philadelphia and London: J. B. Lippincott. 1947. Pp. 1026. £5 10*s*.

THIS large, and in many ways admirable, American textbook of operative surgery has a misleading title. It includes sections on anæsthesia, on the principles of surgical treatment, and on the mouth and œsophagus; but it does not cover the abdomen completely, because the urogenital systems, male and female, are not considered, nor is the abdominal wall. This may perhaps be because it is one in a series of volumes on operative surgery; but it means that the surgeon who wants information on nephrectomy or the treatment of hernia will not get it here. The section on anæsthesia seems too short for the specialist anæsthetist and too theoretical for the man who is compelled by circumstances to administer an anæsthetic and who wants information on how to do it. The chapters on local and regional anæsthesia, however, will be useful to the general surgeon. The section on general topics carries an excellent chapter on the fundamental principles of surgical technique, by Stevenson and Reid, but elsewhere is inclined to give

Digitized by Google

too much detail: it is doubtful, for example, whether the 4 pages illustrating technical apparatus for serum drying are worth their room in a book designed for practising surgeons. The section on the mouth and œsophagus is notable for J. H. Garlock's article on the œsophagus; and the magnificent section on the abdomen, occupying two-thirds of the book, contains chapters by men as well known in England as in America—R. Schindler, A. W. Allen, F. W. Rankin, A. O. Whipple, and others. Perhaps the best chapter in the book is by the late Roscoe Graham on the surgery of the stomach and duodenum; its wisdom, lucidity, and illustrations will commend it as much to the expert in gastric surgery as to the novice.

Nouvelles techniques des traitement de fractures

H. GODARD; R. MICHEL-BECHET. Paris: Doin. 1948. Pp. 406. Fr. 1500.

THIS book gives a full account of recent Continental methods of fracture treatment, which make use of a variety of ingenious mechanical aids to reduction, and various wires or nails of the Küntscher type. Initial chapters describe animal experiments carried out by the authors, which seem barely to prove that the medullary nail is harmless; but the results they record from their practice seem to justify a freer use of the method than is usual in this country. For any surgeon starting to employ it, this book (if it can be obtained) can be strongly recommended, for the authors describe their techniques for almost every fracture of the body with much detail and clarity. They also give full references to other methods of treatment, and in many cases their preference is for the more conservative methods. Far from being rabidly biased in favour of novelty, the book appears to be an earnest account of the methods which the authors, who obviously have great experience, find to give the most satisfactory results.

Hodgkin's Disease and Allied Disorders

HENRY JACKSON, JR., M.D., assistant professor of medicine, Harvard Medical School; FREDERIC PARKER, JR., M.D., associate professor of pathology in the school. New York and London: Oxford University Press. 1947. Pp. 177. 45*s*.

A SPATE of writings bears witness to the fascination which Hodgkin's disease continues to exert. The most recent addition is this monograph from the Harvard Medical School, in which Professor Jackson and Professor Parker analyse a series of cases. Knowledge of the causation of these diseases has not advanced; their clinical and pathological descriptions make no fresh contribution to the mass of factual data already accumulated, a review of which they do not attempt; and they essay no interpretation and offer no general notions to clarify our ideas. Thus it is to their views on the relations between lymphadenoma and allied disorders that their monograph owes its chief interest.

From the diseases which declare themselves by enlargement of lymph-nodes, they have selected three for particular consideration: Hodgkin's disease itself, which they prefer to call Hodgkin's "granuloma"; a condition they have named "Hodgkin's paragranuloma"; and a true neoplasm, Hodgkin's sarcoma. The novelty of "paragranuloma" lies in the term itself, and the authors' apologetic explanation leaves the reader uncertain whether it is intended to convey a close relationship to Hodgkin's disease, or to granulomata in general. Its histological pattern is familiar to workers in this field, and has been given the descriptive title of lymphoreticular medullary reticulosis by Robb-Smith, whose views are accorded no mention in this monograph. "Hodgkin's sarcoma" was employed by Ewing twenty years ago to describe some of the polymorphic neoplasms of lymphoid tissue. The interest of Jackson and Parker's observations lies in their claim that, although Hodgkin's "paragranuloma" commonly pursues a leisurely and relatively benign course, in about one-fifth it is transmuted into the more rapidly progressive "Hodgkin's granuloma." A like transition may occur, they believe, from granuloma to sarcoma. They see Hodgkin's disease as a disorder in which there are three histological varieties, and though either of the more benign may run its course unchanged there is a tendency with the passage of time for it to ascend the scale of malignancy.

There is nothing new about the idea of a change from granuloma to sarcoma; Ewing believed that "Hodgkin's sarcoma" might originate in this manner, though many experienced histologists are still unwilling to accept the metamorphosis. That "paragranuloma" might change into "granuloma" has not been suggested before, perhaps because the "paragranuloma" is not generally recognised. There is a practical importance in establishing or refuting this claim, for a diagnosis of lymphoreticular medullary reticulosis (paragranuloma) is generally held to infer a relatively favourable prognosis, a view which will require revision if one in five is likely to change into true Hodgkin's disease. This tendency for one histological type of disease to change to another they have detected also in the case of giant follicle lymphoma; the frequency of lymphosarcomatous degeneration in this disorder is generally accepted, but these authors have seen, out of 39 cases, 14 change to lymphosarcoma, 7 to Hodgkin's granuloma, 2 to Hodgkin's sarcoma, and 2 to reticulum-cell sarcoma. There is no published experience which accords with this.

The final third of the book is concerned with a review of the disorders allied to Hodgkin's disease, including reticulum-cell sarcoma, lymphocytoma, lymphoblastoma, and giant follicle lymphoma. These sections provide useful descriptions of diseases often neglected in textbooks, but they serve to underline the terminological confusion: for instance, "lymphosarcoma" is used here to denote cases in which there is a single locally invasive and destructive primary tumour.

The monograph is sumptuously produced, but neither its format nor its contents justify the price of 45*s*.

Treatment by Diet (5th ed. Philadelphia and London: J. B. Lippincott. 1948. Pp. 784. 60*s*.).—Prof. Clifford J. Barborka has found it necessary to rewrite, revise, and expand more than half of his book, and the result is striking not only in appearance but in balance and common sense. The foods, the menus, and the measures recommended are American in type, but they can easily be interpreted in more British form.

The World of Learning (London: Europa Publications. 1948. Pp. 824. 60*s*.).—The second and "completely revised" edition of a work first published in 1947, this large book of reference gives detailed information about educational, scientific, and cultural institutions throughout the world, beginning with UNESCO and other international organisations, and going on to national institutions set out under their appropriate countries, arranged alphabetically. The information is so printed that it is easy for the eye to pick it up.

Leaves from the Life of a Country Doctor (2nd ed. London: F. Muller. 1948. Pp. 195. 7*s*. 6*d*.).—This unpretentious and sincere little book of the late Dr. Clement Gunn is really a series of notes and jottings of personal experiences in the course of a life devoted to the service of his fellow men in illness or in trouble; and the record shows how well he carried out his task. He seems to have possessed all the many attributes needed by the country doctor, who can never tell what emergency may next confront him. The book has been edited by Rutherford Crockett.

Manual of Public Health: Hygiene (3rd ed. Edinburgh: E. & S. Livingstone. 1948. Pp. 724. 35*s*.).—The third edition of Currie and Mearns, designed specially for students for the D.P.H. and degrees in hygiene, has been completely revised. It differs materially from the older textbooks in devoting most of its space to preventive medicine as practised by physicians, and only so much to communal sanitation as is required by medical officers of health; so the first chapter is on inheritance and the second and third are on maternity and child welfare and school hygiene. The chapters on inheritance and vital statistics (biometrics) are clear and really interesting, while those on infection and community diseases accord in the main with present knowledge and theory, although there is no reference to the influence of rubella on the embryo. The chapters on infection and prevention accept "disease" as an element of parasitism, which explains both our successes and failures in overcoming endemic infectious diseases.

Digitized by Google

THE LANCET

LONDON: SATURDAY, OCT. 2, 1948

The House Committee

SIX months ago, when the regional boards were grouping their hospitals under management committees, we summarised the opposing arguments in favour of large groups and small ones.[1] We pointed out that if the groups were made large or diffuse the management committees would have to leave much of the day-to-day work to house committees in the individual hospitals; which might mean administration in three tiers instead of the intended two. The groups that have been chosen are in fact on the large side, and in his address last week to the Congress of Physiotherapy Sir WILLIAM DOUGLAS, secretary to the Ministry of Health, said that in England and Wales, besides the 376 management committees, there will be well over 1000 house committees. What functions are these expected to perform? On the one hand they ought not to assume such importance that the management committee loses effective control and becomes merely an intermediate tier; but on the other hand they should provide the benefits that a hospital can obtain only by having a body of volunteers devoted to its particular welfare.

A West Country newspaper has lately reported some remarks on this subject by the chairman of a hospital management committee. "The house committees," he told his audience, "will inspect the hospitals and talk to the patients and staff, and discuss with them the existing facilities and possible ways and means of augmenting or improving them." These words probably sum up pretty well the 1948 conception of the duties of the house committee: it is to be a means, primarily, of ventilating grievances, and thus from year to year bringing about a steadily rising standard of care and attention. And it is quite true that there is room in every hospital for a truly sympathetic group of people who will go round talking to the patients, bringing books and flowers to the lonely, noticing this and that, and passing a quiet word to those in authority. From among such people a few new recruits to the hierarchy who carry genuine management responsibilities can always be drawn with great advantage to the hospital. But if these are to be the members' only duties, what a travesty of the traditional house committee as exemplified in the best of our old hospitals—the inner circle to whom "the House" was a very special concern. Election to the house committee meant (and in many hospitals let us hope will still mean) being one of the privileged few among whom the destinies of the hospital were debated—what should be done about the awkward personality of the latest member of the staff, whether the board should be recommended to embark on the new wing so long needed, whether the friends of the hospital could be relied on to meet the alarming deficit which was beginning to appear, whether the time had come when some trusted sister should be retired—and so on. The chairman of a house committee was a very important person indeed.

Under the new dispensation, authority is vested in the hospital management committees and the regional boards. Therefore, runs the argument, the house committee can only have the residue, the little things that do not matter very much. Yet if the house committee are the people on the spot it seems inevitable that a good deal of real authority should find its way into their hands. Could not this fact be given solid official recognition? Could not the primary responsibility of the house committee be defined as being "to make recommendations to the hospital management committee on all matters affecting the welfare of the hospital"? If the emphasis was thus placed on the idea of responsibility rather than on the little etceteras the whole machine would work more smoothly.

There is more to it than this. No house committee can do its job properly if its members do not understand something at least of the allocation of responsibilities within the hospital. The West Country chairman quoted above suggested that they should talk not only to the patients but to the staff. Much discretion will be needed if this too is to be part of their responsibility. They will need to understand, as the committees of the voluntary hospitals have learnt with much travail, that the dividing lines between lay management and professional responsibilities—medical, nursing, and administrative—are often difficult to discern. The first act of any hospital committee must be to entrust the medical work to the medical staff, the nursing service to the matron, and the managerial executive functions to its executive staff—and then to sit back and allow the machine it has thus created to work, coming to the rescue only when human frailty threatens to cause friction or interruption, or when some major decision is required to adapt the institution to the needs of the community.

1. *Lancet*, 1948, 1, 643.

Beryllium Granulomatosis

BERYLLIUM, or glucinum, is a rare metal mainly obtained from beryl, a beryllium aluminium silicate. The usual cloudy greenish or yellowish crystals found in felspar quarries may be anything up to 18 ft. long; emeralds and aquamarines are clear varieties. The metal is being used more and more in industry because of the remarkable strength of its alloys. Its various salts are incorporated in the powders for lining fluorescent strip-lighting tubes and are also used in atomic-energy research. WEBER and ENGELHARDT[1] in 1933 discovered lung symptoms among workers extracting beryllium from the ore, and soon afterwards FABRIONI,[2] of Milan, exposed guineapigs to the fumes of beryllium carbonate and produced lung lesions which he called "berylliosis." Then Russian workers, led by GELMAN,[3] observed a severe pneumonitis in people exposed to fumes

1. Weber, H. H., Engelhardt, W. E. *Zbl. Gewerbehyg. Unfallverhütung.* 1933, 10, 41.
2. Fabrioni, S. M. *Med. Lavoro*, 1935, 26, 297.
3. Gelman, I. *J. indust. Hyg.* 1936, 18, 371. Also supp. to Occupation and Health. Geneva: I.L.O. 1938.

Digitized by Google

in the extraction of beryllium from its fluorides. This illness occurred in two phases—an immediate phase resembling metal fume fever, followed about 4 days later by a severe bronchiolitis. GELMAN regarded the first phase as due to beryllium fume and the second to the action of fluorine. German investigators [4] also reported on beryllium poisoning during the late war. But since 1943 the United States has had the fullest experience of the noxious effects of beryllium and its compounds, and the American delegates read several papers on the subject at the International Congress on Industrial Medicine.[5]

The pneumonitis produced by beryllium may be acute or chronic. The chronic form has a delayed onset with dyspnœa and loss of weight. At the recent congress Dr. C. R. WILLIAMS analysed about 100 cases in relation to the industries where they occurred. As Dr. AGATE points out on p. 530, most but not all of the acute cases came from factories where beryllium was being extracted from the ore, whereas most of the delayed cases came from the fluorescent-lamp industry in which the workpeople had inhaled dust containing zinc beryllium silicate with manganese tungstate. Prof. W. MACHLE, who had studied 60 chronic cases, described the pathological changes and chemical findings in the tissues of fatal cases. The characteristic lesion of the chronic or delayed pneumonitis is a granuloma in the lungs which produces X-ray shadows resembling those of some forms of pneumoconiosis, miliary tuberculosis, or sarcoidosis. These granulomatous changes are also found in the liver, and Dr. PETER NASH reported some cases of subcutaneous granulomata occurring in people who had cut themselves on broken fluorescent lamps. Histologically these granulomata resemble the skin lesions which develop in cases of pulmonary granulomatosis; they are also very similar to sarcoidosis of the skin, though the two conditions are probably not identical. Prof. A. POLICARD'S [5] experiments have shown that beryllium sodium fluoride dusts provoke violent pulmonary œdema, whereas beryllium oxide causes histiocyte pneumonia, granulomatous nodules, and cellular thickening of the alveolar walls.

Dr. AGATE gives details of probably the first case of delayed chemical pneumonitis in a beryllium worker to be reported in this country. This was in a laboratory worker who developed cough and dyspnœa and lost a great deal of weight three years after being exposed to the dust of zinc beryllium manganese silicate while working on the development of fluorescent lamps. X-ray examinations of his lungs showed extensive bilateral reticular and nodular shadows. Granulomatous lesions were found in the liver without biochemical evidence of disturbed liver function. Dr. AGATE remarks that the commercial use of beryllium has expanded so greatly in Great Britain during the last three years that further cases may be expected, and he suggests that the best way to prevent poisoning is to substitute less harmful compounds for beryllium. Treatment of the disease is ineffectual, the prognosis is bad, and the disability is serious and permanent; so legislation to provide for compensation might be considered even before more cases are discovered. The American evidence against beryllium is certainly weighty, and no doubt the authorities are taking steps to prevent further examples of the acute and chronic diseases which it may cause.

4. Meyer, H. E. *Beitr. klin. Tuberk.* 1942, **98**, 388. Wurm, H., Rüger, H. *Ibid*, p. 396.
5. See *Lancet*, Sept. 25, p. 506.

Treatment of Hæmolytic Disease of the Newborn

THE several clinical conditions arising from rhesus incompatibility between mother and fœtus, now grouped together as hæmolytic disease of the newborn, can most readily be diagnosed with the direct anti-globulin test devised by COOMBS, MOURANT, and RACE.[1] According to the Medical Research Council memorandum [2] reviewed in these columns last week, it is doubtful whether this test is ever negative in true hæmolytic disease—in fact, the test may be positive although the infant never develops signs of a hæmolytic anæmia.[3] In this issue MOLLISON and CUTBUSH report that in a series of cases seen by them, and diagnosed by the anti-globulin test, almost a quarter of the infants were so mildly affected as not to require any treatment. Thus in selecting cases for treatment it is essential to assess their severity, and the earlier this is done the better. By estimating the hæmoglobin and bilirubin content of a sample of cord blood it is possible at least to pick out the cases which are likely without treatment to pursue a mild course. For the sake of the many clinicians who must come to a decision without the help of elaborate laboratory data, it is suggested that the onset of jaundice within 12 hours of birth in an infant with a positive direct anti-globulin test warrants immediate treatment.

Two methods of treating hæmolytic disease of the newborn are now widely practised. The first, which obviously demands antenatal diagnosis, is premature termination of pregnancy. This clearly holds out the only hope of preservation for those infants who would otherwise die in utero during the last few weeks of pregnancy. Moreover, since some cases survive until, say, the 37th week of pregnancy and then die in utero, there are probably others which might be irreparably damaged by the 40th week and yet at the 37th week are still capable of surviving if removed from the supply of Rh antibody. Against this view it might be argued that an infant who, if left in utero till term, would be born dead or dying, is probably already in a critical condition at the 36th week of pregnancy, and the extra hazard of prematurity might well outweigh the slight gain of a reduced exposure to anti-Rh. It must be remembered that infants may already be so badly damaged by the 26th week of pregnancy as to die of hæmolytic disease.[4] There are as yet no published records which will tell us whether premature termination of pregnancy saves the lives of any infants with hæmolytic disease, but doubtless attempts are being made to obtain this information.

The second method of treatment is the transfusion of Rh-negative blood. LEVINE and his co-workers,[5] when they first discovered the rôle of the Rh factor

1. Coombs, R. R. A., Mourant, A. E., Race, R. R. *Lancet*, 1946, i, 264.
2. Mollison, P. L., Mourant, A. E., Race, R. R. M.R.C. Memo. no. 19. London, 1948. See *Lancet*, Sept. 25, p. 502.
3. Pickles, M. M. Dissertation for degree of D.M. Oxfd, 1947.
4. Gilmour, J. R. *Arch. Dis. Childh.* 1944, **19**, 1.
5. Levine, P., Burnham, L., Katzin, E. N., Vogel, P. *Amer. J. Obstet. Gynec.* 1941, **42**, 925.

Digitized by Google

in the disease, pointed out that transfusion of Rh-negative blood was far more efficacious than that of Rh-positive blood. Later, MOLLISON [6] demonstrated that Rh-positive erythrocytes might be completely eliminated within 2–3 days of transfusion, whereas Rh-negative ones were only slowly eliminated over 100 days or so. He noted that a case could be made out for transfusing Rh-negative blood even though the infant was not anæmic; because, if sufficient Rh-negative blood was transfused, the infant's peripheral blood might after a few days contain only Rh-negative erythrocytes, so transfusion evidently depressed blood-formation by the bone-marrow. The diminished production of Rh-positive erythrocytes might be beneficial, though this was difficult to prove. WALLERSTEIN [7] carried this approach to its logical conclusion when he suggested withdrawing some of the infant's blood from the sagittal sinus during the transfusion, to secure a more rapid and complete replacement. Oddly enough, the same treatment had been suggested and applied by HART [8] 20 years earlier. Since WALLERSTEIN revived interest in exchange transfusion several techniques have been advocated. WIENER [9] bleeds the baby from the radial artery and injects blood into its saphenous vein at the ankle. DIAMOND [10] withdraws and injects blood through a fine plastic catheter passed up the umbilical vein within 12 hours of birth. Others [11 12] use the same form of catheter but pass it via the great saphenous vein into the femoral vein and thence into the vena cava; this method involves a wound in the groin and thus seems best restricted to cases where the umbilical vein cannot be catheterised. WALLERSTEIN, who at first proposed applying exchange transfusion only to severely affected infants, later,[13] encouraged by preliminary results, suggested its wider use as a prophylactic measure immediately after birth to prevent the development of the "toxic state." This brings one to the most controversial aspect of the pathology of hæmolytic disease. What is it that causes an infant who may be vigorous at birth to deteriorate rapidly 48 hours later and die within a further 24 hours? At autopsy, damage to the brain and liver are often found, and WALLERSTEIN goes so far as to say that kernicterus probably occurs only after such liver damage. However that may be, it is difficult to resist the feeling that for 12–24 hours after birth these infants are not irreparably damaged and that the complete arrest of blood breakdown might save at least a few of them.

From their trial of exchange transfusion, MOLLISON and CUTBUSH are careful to conclude that the value of the method in reducing mortality and morbidity remains unproved. Nevertheless, from their report it seems at least as satisfactory as other methods of treatment, and it offers the tangible advantage of rendering a series of transfusions unnecessary. In deciding whether to adopt exchange transfusion as the treatment of choice it is wise to avoid a hasty judgment. The very variable severity of the disease and the consequent large effect of selection makes it almost impossible to contrast one series with another; only a self-controlled series is likely to provide a decisive answer. Meanwhile, provided exchange transfusion is not too dangerous—and in severe cases of hæmolytic disease of the newborn the mortality is high enough to justify drastic measures—it should be given a long trial on cases collected so that this method of treatment can be compared with others. In view of the heavy demands on the time of clinicians and laboratory workers which proper trials of this kind involve, it seems best for the present to leave exchange transfusion in the hands of special centres and to transfer all cases to central hospitals. This, in turn, necessitates the routine antenatal diagnosis of hæmolytic disease of the newborn. The encouragement of early diagnosis will be a valuable by-product of exchange transfusion and this in itself is likely to raise the standard of treatment.

6. Mollison, P. L. *Arch. Dis. Childh.* 1943, **18**, 161.
7. Wallerstein, H. *Science*, 1946, **103**, 583.
8. Hart, A. P. *Canad. med. Ass. J.* 1925, **15**, 1008.
9. Wiener, A. S., Wexler, I. B. *J. Pediat.* 1946, **31**, 1016.
10. Diamond, L. K. *Proc. R. Soc. Med.* 1947, **40**, 546.
11. Arnold, D. P., Alford, K. M. *J. Pediat.* 1948, **32**, 113.
12. Buhot, S. *Rev. Hématol.* 1948, **3**, 92.
13. Wallerstein, H. *Amer. J. Dis. Child.* **73**, 19.

Annotations

RESEARCH

"IT is orthodox to pay lip service to research; but I know that many balanced and intelligent men are sceptical in their hearts about the justification of research in medicine, by men who are not geniuses, in laboratories no more than adequately equipped, in places far from the great centres of learning." Prof. F. M. Burnet, F.R.S.,[1] believes that most research-workers at one time or another doubt the social justification of their career. "We work hard and conscientiously, we make some small but significant discovery, and we publish a paper about it. That paper probably costs the community a thousand pounds, and sometimes we wonder whether the community has been given its money's worth." Yet, though the immediate value may seem small, none of the great discoveries of scientific medicine could have come without the guidance provided by hundreds of thousands of such day-to-day investigations.

"Behind Fleming was all the knowledge of bacteriological technique that Pasteur, Koch and their followers had developed—and we must not forget that the agar base of the historic plate on which that mould spore of Fleming's landed was there because Frau Hesse, whose husband was one of Koch's men, used agar to make her jellies set better and she had got the recipe from a cousin in Java! And Florey would be the first to admit from what multitudinous sources came the knowledge of how penicillin might be isolated from the crude juice in which the mould had grown or how its curative activity might be measured."

Dr. Burnet contrasts the two contending doctrines of the nature and social function of scientific work:

"The communist doctrine is that science is and always has been a by-product of economic necessity and that its social function is wholly to assist in the efficient satisfaction of human needs. The traditional academic view, still ably supported, is that the search for knowledge is an intrinsically valuable activity to be pursued according to certain established rules and finding its greatest success and justification in the emergence of a more and more intellectually satisfying picture of the universe."

Regarding neither of these views as extreme or ridiculous, Dr. Burnet thinks that they can and must be fused. He holds that the task of science is "to provide a general body of accurately established knowledge, from which can be drawn with increasing ease and completeness the information needed to allow the efficient satisfaction of any specific human requirement." Knowledge has to be built into an integrated pattern; and "the real task of the men engaged in research in hospital wards or university laboratories is not to seek

1. *Med. J. Aust.* Sept. 11, p. 281.

Digitized by Google

a cure for cancer or rheumatism, but to play their part in clearing up the uncertainties and closing the gaps in the medical sciences."

Writing of clinical research, Prof. L. J. Witts [2] wisely insists on the need for time and space in which to perform it. After the 1914–18 war the university clinical departments were diverted from research to teaching; and there is some danger, he thinks, that they may now be diverted to regional organisation. Clinical research is bound to suffer if the National Health Service makes excessive demands on the universities for technical and administrative help. Too many people with the power to make appointments, Professor Witts finds, regard clinical research as a sort of intelligence test, indicating whether a man is suitable to receive a chair or a hospital appointment: they hardly think it should engage his time after he has been given the job. "The fact that a single clinical scientist like Colebrook can do more for the relief of suffering in obstetrical and surgical emergencies than a hundred practising specialists or administrators makes little impression." Professor Witts deplores the lack in this country (compared with the United States) of "an abiding faith in clinical research as the most important business in which a hospital can be engaged."

TUBERCULOSIS IN INDIA

TUBERCULOSIS is one of the greatest scourges of India. Lady Mountbatten,[3] in her presidential address to the Tuberculosis Association of India, quoted estimates of 500,000 deaths and 2,500,000 new cases each year. In 1947, partition duplicated the responsibility for dealing with this as with other pestilences, while dividing the available resources. The report of the Tuberculosis Workers Conference,[4] held in New Delhi a few months before partition took place, provides a base-line from which subsequent progress can be measured. We in Britain complain of bed shortages, but India has only 8000 institutional beds for tuberculosis and a corresponding lack of clinics, equipment of every kind, personnel, and funds. A small devoted band of tuberculosis workers face these handicaps and also those of poverty and ignorance. Yet there are few methods used in the west which are untried in India. For example, 'Promin' has been under trial in pulmonary tuberculosis; the firm of Bata carried out an experiment in B.C.G. inoculation on its employees, with good results, and it is hoped to begin widespread vaccination next year. A follow-up of cases in Lahore from 1940 to 1945 strikingly illustrates the conditions with which the Indian tuberculosis worker has to deal—the appalling overcrowding often making isolation impossible, the ubiquitous malnutrition, the absence of sanitary facilities, and, not least, the absence of notification and of reliable statistics of births and deaths.

The partition of India was followed by outbreaks of communal violence on an unprecedented scale, and by mass migrations that can seldom have been exceeded. Hundreds of thousands perished during those first few months, and millions are still living in primitive camps under conditions of overcrowding and privation even worse than they had previously experienced. Dr. Jivraj N. Mehta, outlining the association's future programme, declared that "ultimately it is the economic improvement of the community which can provide the necessary bulwark against disease." While the individual worker may struggle heroically on a tiny sector of the front, the problem of tuberculosis in India will remain insoluble until the land is at peace and until the general standard of living is vastly improved.

2. *Brit. med. J.* Sept. 4, p. 455.
3. Proceedings of the Ninth Annual General Meeting, 1948. Tuberculosis Association of India, 20, Talkatora Road, New Delhi.
4. Transactions of the Fourth Tuberculosis Workers Conference, New Delhi, 1946.

AMŒBÆ IN BRITAIN

A CORRESPONDENT lately asked for the evidence on which we remarked [1] that "10–20% of the ordinary adult population of England carry amœbæ which are *E. histolytica* or which cannot be distinguished from it." The occurrence of intestinal protozoa in the inhabitants of Great Britain was exhaustively studied by Dobell [2] in 1921; and little further information has since been added. About 3146 apparently normal people from different parts of England were examined, mostly by looking at a single specimen of fæces; none of these people had ever been abroad. Cysts of *Entamœba histolytica* was found in 107—i.e., 3·4%. However, Dobell estimated that a single examination probably detects only about a third of the cases, so the true percentage incidence was probably 7–10% for *E. histolytica*, 36–54% for *E. coli*, and 9–13% for *Endolimax nana*. A history of diarrhœa seemed to be no commoner in the carriers of *E. histolytica* than would be expected in any sample of the population. Apparently the infection is acquired at an early age and persists for most of life. Endemic infestation of the same order probably occurs in all parts of Great Britain, and also in France, Holland, Germany, and (presumably) other countries of Europe. It has probably existed for centuries in Britain and yet amœbic lesions of the intestine or liver are rarely found in people who have lived here all their lives; so the pathogenic effects of our native amœbæ must be slight except in a few specially susceptible individuals. The practical significance of this knowledge is twofold: (*a*) the fact that a patient has never left this country does not exclude the possibility of amœbic infection, (*b*) the demonstration of *E. histolytica* cysts in a patient's stools is not strong evidence that his symptoms are due to amœbiasis.

TISSUE HEATING BY MICROWAVES (RADAR)

SINCE d'Arsonval in 1890 showed that high-frequency electrical currents of 10,000 cycles per second heated the tissues without causing any muscular contractions, the therapeutic applications of this technique have been pursued relentlessly. Step by step the frequency was increased and long-wave diathermy with 3 megacycles per sec. opened a new epoch in physiotherapy, only to be succeeded by short-wave diathermy with a threefold frequency. Then inevitably there arrived ultra-short and now finally radiations of frequency 3000 megacycles per sec. (wave-length 10 cm.) are being used.[3] The Mayo clinic workers call this microwave therapy or "microkymatotherapy." The microwaves are on the long wave-length side of ordinary heat; but heat waves do not possess the desired ability to penetrate the tissues.

Power is the all-important factor, and it has taken about ten years to get enough power with these latest oscillating circuits to make it worth applying the resultant energy to the end in view—i.e., local heating. The solution was found in the multicavity magnetron tube, devised in Britain and developed in America, with an average power output of 1000 watts and a peak of a million. The radiation emitted by this tube can be reflected, refracted, or focused by suitable lenses like a spotlight, so its clinical use should be simple. When radiation of this frequency is passed through water at body temperature, the proportion of the radiant energy absorbed is some 7000 times as great as with the 27 megacycles per sec. radiation now commonly used for short-wave diathermy. Since the tissues are largely

1. Annotation, Aug. 14, p. 262.
2. Dobell, C. A Report on the Occurrence of Intestinal Protozoa in the Inhabitants of Britain, with special reference to *Entamœba histolytica*. *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 59, 1921.
3. Krusen, F. H., Henik, J. F., Leden, W., Wakim, K. G. *Proc. Mayo Clin.* 1947, **22**, 209.

Digitized by Google

composed of water, this means that there will be a correspondingly greater absorption of energy by the tissues. The local heat produced in the body by this kind of energy brings about an increase of venous return and a vasodilatation through local reflex mechanisms and direct metabolic effects. The heart-rate may be increased by speeding up the generation and propagation of impulses through the sino-auricular node. On the basis of the experimental tests, the Mayo Clinic have been carrying out clinical studies with microwaves for the past year.

NEUROSURGICAL SERVICE

IN their new organisation by regions, the British hospital services form a clear pattern, in which each segment gathers strength from, or gives support to, its neighbours. Even so, there are still dangerous gaps, particularly in the services which are least often called for or most difficult to supply; and perhaps the most notable of these is neurosurgery.

The Society of British Neurological Surgeons, like the Society of Thoracic Surgeons,[1] has produced its own design for the future[2]; and this shows how pitifully deficient are the present resources. The expansion of neurosurgical work, like that of chest surgery, has been swift; and this means that there are neither enough hospital beds nor enough trained surgeons. The late war brought a great increase in the number of beds set aside for this specialty; but even now large areas have no neurosurgical centre whatever. The report suggests that the aim should be to supply for every million people a centre having 50–60 beds (though some hold that 80–100 are needed). The regions named as specially needy are South Wales, the eastern counties, Scotland, Northern Ireland, and London; and in addition area centres, with some 25 beds each, are proposed for the East Midlands, the East Riding of Yorkshire, north Lancashire, and the south-west. New centres, says the report, should be placed on land shared with a teaching, or at least a general, hospital. For full use of resources, convalescent beds should, if possible, be in the same hospital; but, if this advantage can be won only by the exclusion of the whole unit from the general hospital, then it should be foregone. The committee, insisting that surgical neurology is a proper subject for the undergraduate's clinical training, holds that units of not less than 25 beds should be installed in teaching hospitals.

Considerable thought has been given to the training of future neurosurgeons. This, in the committee's view, should be in two stages. The first is that of general training in which the young graduate spends a year in junior resident appointments, a second year in whole-time study of the basic sciences, and a third as senior house-surgeon or R.S.O. After taking the F.R.C.S. he will, the report points out, become a better recruit by doing another year in general surgery. "We say this from the knowledge that the best and most telling experience in general surgery is not usually to be had until this diploma has been acquired." The second stage—that of special apprenticeship—would take at least a further four and a half years, the trainee spending a year each in work as senior house-surgeon in neurosurgery; in neurophysiology or an alternative subject (including six months in medical neurology); in neurosurgery as a registrar; and finally as a registrar with work outside the hospital as a domiciliary consultant.

Not all neurologists, and perhaps not every neurosurgeon, will agree with the committee in maintaining that head injuries should necessarily be treated in the surgical unit. In the late war the largest Service hospital for medical and surgical neurological cases adopted the practice of admitting all closed head injuries to the medical wards. The virtue of this arrangement was twofold: it saved surgical beds; and from the start of treatment these cases were in the hands of the physicians, whose interests perhaps qualified them better to take charge up to and including convalescence. The occasional intervention by the surgeon—for example, to make a burr-hole—which is cited as a reason for surgical control, was seen as an incident in a disorder which was essentially medical; and, since the committee visualises medical and surgical units working side by side in a single specialised department, there seems to be no practical reason why this view should not prevail in the future. The further contention that few physicians have displayed much interest in head injuries should make neurologists look to their laurels.

1. See *Lancet*, 1948, i, 801.
2. Society of British Neurosurgeons, Planning Committee 1945–47: Notes on the Neurosurgical Needs of the Population and the Training of the Neurosurgeon.

WAR RESEARCHES ON THE CORNEA

SOME of the work undertaken for urgent reasons during the war is only now being published. Two monographs appearing within the last few months describe investigations, by teams in the United States and in England, on the mode of action of war gases on the eye.[1] Both reflect the high academic standard of research favoured by the Allied policy of employing civilian scientists to study Service problems. Though largely concerned with the effects of substances unlikely in ordinary circumstances to come in contact with the eye, the thirteen authors have done much to set knowledge of the biochemistry and histopathology of the cornea on a sounder basis. The Americans directed their attention mainly to biochemistry, and the English mostly to cellular reactions; but both groups start with fundamentals applicable to the study of any chemical injury to the cornea. They point out that the action is determined not only by the toxicity of the material, but also by its physical power of penetration. They emphasise the importance of SH groupings in reaction with proteins, and by bringing the problem of injury into the realm of enzyme inhibitions and activations they have advanced ophthalmic pathology far beyond its previous boundaries.

The metabolism of the cornea has been studied in great detail. The functions of its various layers have been separated. Attention has been drawn to such phenomena as the inability of the stroma to take up oxygen or to utilise lactate or pyruvate, the great capabilities of the epithelium, and the existence of a hydrogen transport system from stroma to epithelium. The epithelium-stroma boundary, probably a protein-lipoid multilayer, is the seat of many important activities, and the circumstances in which the epithelium becomes loosened have been carefully examined. Oxygen is essential for this loosening, which does not occur anaerobically even after poisoning of enzyme systems with various toxins. The effects of chemical and physical agents (e.g., mustard gas, colchicine, ultra-violet light, and X rays) on the mitosis and on nuclear fragmentation have also been worked out, and so have the effects on the stroma and epithelium of a large number of chemicals not related to war.

The English team, who began work nearly three years before the Americans, gave its attention largely to the clinical appearances of chemical injuries and to the histology of various types of healing. The problem of avascular healing of the corneal stroma and of the epithelium has puzzled ophthalmologists for many decades and the experiments described in the *British*

1. Studies on the Physiology, Biochemistry, and Cytopathology of the Cornea in relation to Injury by Mustard Gas and Allied Toxic Agents. *Bull. Johns Hopk. Hosp.* 1948, **82**, no. 2.
An Experimental and Clinical Study of the Reaction of the Anterior Segment of the Eye to Chemical Injury with special reference to Chemical Warfare Agents. *Brit. J. Ophthal.* monograph, 1948.

Digitized by Google

Journal of Ophthalmology monograph go far to explain it. No such detailed intra-vitam long-term observations of corneal damage have previously been published and many conditions of vascularisation and degeneration are elucidated. This work has greater immediate clinical application than have the biochemical experiments, and the illustrations (photographs, photomicrographs, and slit-lamp drawings) should prove suggestive to clinicians examining obscure corneal conditions.

Parts of this monograph have already appeared as isolated papers, but their collection into a single volume will be an advantage. It is to be hoped that the new techniques and experimental methods described will be fully applied.

PTERINS FOR LEUKÆMIA

THE synthesis of pteroylglutamic (folic) acid has enabled the therapeutic uses of this previously unimportant group of substances to be thoroughly explored. Starting from the original substance, completely artificial compounds have been prepared and applied to the treatment of diseases like sprue and pernicious anæmia, which are not at present considered to be deficiency diseases. The use in malignant disease of the artificial pteroyldiglutamic acid (diopterin), and of pteroyltriglutamic acid (teropterin), a synthetic compound which does occur in nature, has already been mentioned in these columns.[1] Lately Farber and others[2] have been studying the effect of the synthetic compound 4-aminopteroylglutamic acid (aminopterin) in children with acute leukæmia. Aminopterin is a folic-acid antagonist—i.e., it prevents folic acid from exerting its growth-promoting property for *Streptococcus fæcalis* R. Its use was suggested by the observation that when diopterin or teropterin was given to acute leukæmic children the disease seemed to be actually accelerated and the infiltrations seen at necropsy were unusually extensive. The first folic-acid antagonist to be tried was pteroylaspartic acid. This was given intramuscularly to a child dying from acute myelogenous leukæmia; all the clinical findings and the bone-marrow biopsy were typical. The patient received 8 daily doses without any effect on the clinical course and died on the 8th day; but at necropsy the bone-marrow was found to be hypoplastic with few immature cells. Further studies with pteroylaspartic acid encouraged a more extended experiment with aminopterin—a much more powerful folic-acid antagonist.

Farber and his co-workers now report the results of aminopterin treatment in 16 patients, of whom 4 died and 2 showed no response. In the remaining 10, however, the response could be classed as favourable, over an admittedly short period of three months. In these cases the white-cell count, if raised, tended to return to normal levels; the immature leucocytes in the peripheral blood sharply decreased or even disappeared. Anæmia became less and low platelet-levels rose. In the bone-marrow the response was sometimes a decrease, sometimes a total disappearance, of leukæmic cells, but the marrow became hypoplastic in some cases. Enlargement of liver, spleen, or lymph-glands steadily decreased. This all sounds very promising, but there is another side to the picture. The remissions appear to be only temporary, the longest so far lasting 43 days. Then there are toxic side-effects, like a troublesome stomatitis not always controllable by injection of crude liver extracts, and others—more serious—such as the toxic depression of all blood-forming tissues, refractory to treatment. The *New England Journal of Medicine*[3] reminds us of that often forgotten phenomenon, the spontaneous remission, which is not uncommon in acute leukæmia of children and has been known to last as long as thirteen months; but every patient in whom the diagnosis was certain has eventually relapsed with rapidly fatal results. Secondly, it points out that cautious reports—like that of Farber and his colleagues—are seized on by the lay press, suffer a marvellous sea-change of distortion, and emerge as positive hopes of cure for a certainly fatal disease. The expert will not be influenced, but the general physician who is not familiar with the pitfalls may be tempted to try these new substances in any case he even suspects of being leukæmia, the idea being to give treatment as early as possible to grasp the maximum chance of success. Thus patients who never had leukæmia at all are reported as "successes." These warnings are fully justified. The diagnosis of acute leukæmia in the early stages is a job for the expert—and even he may make mistakes. Yet, once established, there are few diagnoses that carry a death sentence with such finality. The nitrogen mustards and their like have already proved useless in acute leukæmia. The action of these pterins may perhaps be something different from mere destruction of abnormal cells, and further experience with aminopterin, or less toxic similar substances, may give us a real clue to the nature and effective control of this unpleasantly fatal disease.

1. *Lancet*, 1948, i, 184.
2. Farber, S., Diamond, L. K., Mercer, R. D., Sylvester, R. F. jun., Wolff, J. A. *New Engl. J. Med.* 1948, **238**, 787.
3. Editorial, *Ibid*, p. 814.

THE LAWS AND THE JUDGES

OUR remarks, on Aug. 21, about the zeal of judges for the retention of capital and corporal punishment, find support in a paper by Finer,[1] entitled Recurrent Characteristics in Opposition to Reform. He cites *Hansard* to illustrate how true to type the arguments in favour of barbarous punishments appear to run:

> "Mr. Yorke spoke in favour of the retention (of drawing and quartering) for the following reasons. The punishment was as ancient as the Law of England, as ancient as any of those laws which secured the safety of property and which no rational man would wish to alter. . . . The greatest punishments should be reserved for the greatest crimes. When we consider the many evils with which we were threatened from our superabundant population and from other fearful causes, could we consider ourselves as entering upon a new golden age . . . ? It was extraordinary that the gentlemen should feel all the pity for the culprits, and none at all for the evils that the public might suffer. How many houses would be burned, how many murders perpetrated, how many rapes committed ? "

It has often been customary to discredit penal reform by identifying it with revolution, and on this distant occasion several speakers pointed out that the abolition of corporal punishment in France was one of the earliest acts of the French Revolution. Some of the arguments advanced in the recent Lords' debate on capital punishment recall those used by "Black" Sir John Sylvester, Recorder of London in 1816, when he sentenced a boy of ten to death for stealing. Similarly, Lord Templewood's speech contained an echo of the following words of Romilly, his forerunner in reform:

> "I call upon you to remember that cruel punishments have an inevitable tendency to produce cruelty in the people. You may cut out the heart of a sufferer and hold it up to the view of the populace, and you may imagine that you serve the community; but the real effect of such scenes is to torture the compassionate and to harden the obdurate. In times of tranquillity you will not diminish offences by rendering guilt callous—and in times of turbulence fury will retaliate the cruelty which it has been accustomed to behold."

Dr. R. H. PARRY, medical officer of health for the city and port of Bristol and professor of preventive medicine in the University of Bristol, has been elected president of the Society of Medical Officers of Health.

1. Finer, M. *Howard Journal*, 1948, **7**, 3.

Digitized by Google

Special Articles

ORGANISATION OF AN ARTHRITIS CLINIC

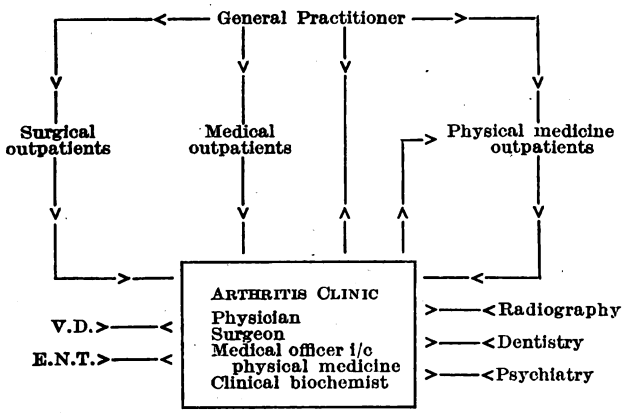
A. A. McINTOSH NICOL M.D. Aberd., F.R.C.P.
W. GRANT WAUGH M.A., M.D. Edin., F.R.C.S.E.
IAN C. COWAN M.B., B.Sc. Aberd.
JOHN HARKNESS M.B., B.Sc. Glasg.
From the Sunderland Royal Infirmary

THE investigation and treatment of the rheumatic diseases is recognised as an outstanding problem in medicine. Although much progress has been made in recent years in the pathology and consequently in the treatment of non-articular rheumatism, little progress has been made in determining the ætiological agent in rheumatoid arthritis; and the methods of treatment of this disease, apart perhaps from the acidification of joints, have for some time remained stationary. A possible reason for the lack of advance is that patients have been treated by the physician, the surgeon, or the physical-medicine specialist individually. Each of these has tended to concentrate on his own part of the treatment: there has been no coördinated combined attack by specialists equipped for the purpose. That such an attack is necessary is shown by the statistics issued by the British Rheumatic Association:

1. Deaths from all forms of rheumatic diseases in 1938 totalled 6000.
2. Known rheumatic sufferers in the British Isles total 4,000,000.
3. 32,250,000 days' work is lost each year through rheumatism.
4. In 1938 £17,000,000 was spent on sick benefit for sufferers from rheumatism.

Because the area served by Sunderland Royal Infirmary contained so many patients suffering from rheumatism of all forms it was decided to establish an arthritis clinic so that these could be investigated fully and the various methods of treatment could be tested. The organisers of this clinic believe the problem can be tackled only by a team of specialists, working in such a way that the patient's condition is assessed, and the treatment is planned, by *the team in consultation*. With this basic principle in mind the arthritis clinic began work in 1947 with four specialists—a physician, a surgeon, a medical officer in charge of physical medicine, and a clinical biochemist. To this team is added from time to time, according to needs of the case, a radiologist, an ear, nose, and throat surgeon, a dental surgeon, a psychiatrist, or a venereologist.

The organisation of the clinic may be illustrated thus:



The patient is sent by the general practitioner to any one of the various outpatient departments, from which the physician or surgeon refers him to the arthritis clinic. (The general practitioner has also direct access to this clinic.) During the first attendance a detailed medical and family history is taken, and the patient is also interviewed by the almoner, who makes out a confidential report on home conditions, employment, family income and diet. The patient is then seen by the physician together with the medical officer in charge of physical medicine, and a complete medical examination is carried out, including a detailed examination of the locomotor system with special reference to the joints involved. Exact measurements of the amount of movement in the joints are noted, and an estimate of the activity of the disease process in the joints is made. Any possible focus of infection is searched for; skiagrams of chest, sinuses, and involved joints are requested as a routine. If a focus of infection is found—e.g. chronic cholecystitis, septic teeth, or sinus infection—the patient is passed to the appropriate specialist, to be returned to the clinic when that focus has been eradicated. In addition to the usual blood and urine examinations, special emphasis is placed on biochemical investigations to determine the systemic reaction to the disease process. Erythrocyte sedimentation, plasma viscosity, gold flocculation, and plasma alkaline phosphatase are estimated as a routine, and urinary 17-ketosteroids in suspected ankylosing spondylitis. Thus in the first visit to the clinic a complete investigation is made.

At the second visit, for which an appointment is given, all the results of the various tests are to hand, the condition is finally assessed, and treatment prescribed by the members of the team in consultation. If an intensive course of physical therapy is indicated, the patient is taken over by the medical officer in charge of physical medicine, who follows the case through his department, sending the patient back to the central clinic from time to time for review. Special courses such as chrysotherapy or vaccine therapy, or general medical treatment, are arranged in the same way. From the appropriate specialist the patient receives the treatment prescribed by the arthritis team, and returns for review periodically. Those on chrysotherapy are seen weekly, and routine blood tests are made every three weeks, or more frequently if need be. Urine examinations are carried out weekly before each injection of gold or heavy metal. Patients requiring manipulation, splintage, or acidification of joints (Waugh) are seen by the surgeon and medical officer in charge of physical medicine together, and what may be termed a tactical plan of attack is drawn up.

By this method a period of one week usually elapses between the patient first being seen at the clinic, and the commencement of treatment.

Owing to the shortage of beds and nursing staff, fewer than 1% of the patients passing through the clinic are admitted to hospital; but our experience shows that however desirable it is to have inpatient accommodation, a great deal can be done for a very large proportion of patients attending only as outpatients. In the acute cases which need admission the same routine of preliminary investigation by the team, and planned treatment by the team, is strictly followed.

When the patient has passed through the clinic and received a course of treatment he or she is asked to return periodically for review. Attached to the clinic through the physical-medicine department there is a resettlement officer of the Ministry of Labour. Where a change of employment is indicated, or where return to the original occupation is impossible, the resettlement officer is consulted and an attempt is made to re-employ the patient, or to retrain him so that he can once more be a useful member of the community.

We hope later to publish the findings of this clinic, assessing the value of the various methods of investigation and treatment.

Digitized by Google

INFERTILITY

FAMILY PLANNING ASSOCIATION'S CONFERENCE

A conference on infertility, arranged by the Family Planning Association, was held at Exeter on Sept. 25 and 26.

Congenital Absence of the Vas

Mr. DONALD H. YOUNG, F.R.C.S.E. (Liverpool), described cases of congenital absence of the vas deferens. In the first he had seen, the semen was found to contain no spermatozoa, though biopsy of the testicle showed that spermatogenesis was normal. At cystoscopy, the bladder and ureteric orifices appeared normal, but no ejaculatory ducts were visible; and at operation the vasa deferentia were found to be represented by thin fibrous cords. Fructose is normally present in semen, and is formed in the seminal vesicles; its absence implies disease of the vesicles or absence of the vas. Up to 1940 some 30 cases were noted in Germany among patients undergoing compulsory sterilisation under the Nazis; these amounted to 0·5% of the total number sterilised. A few cases have been reported in the United States since 1945. Cases of obstruction of the ejaculatory ducts give the same seminal findings but can be distinguished by the fact that the vas is palpable.

Similar cases were described by Dr. G. L. FOSS (Bristol), Dr. H. A. DAVIDSON (London), and Mr. LINTON SNAITH, F.R.C.S. (Newcastle); and by Dr. T. MANN, (Cambridge), who added that human semen contains, besides fructose, something under 1% of citric acid. This derives, in man, from the prostate, and might, he suggested, be used as a measure of prostatic secretion. Mrs. CLARE HARVEY, who has been doing fructose estimations in semen since last February, said that in five or six specimens showing azoospermia which she examined fructose was present, whereas the only specimens without fructose showed normal sperm counts. Dr. MANN pointed out that if an occlusion is above the seminal vesicles fructose will be present in the semen: moreover human semen is not of a constant chemical composition; it varies, in the same subject, from specimen to specimen.

Supravital Staining

Miss ANITA MANDL described a method of supravital staining with buffered soluble blue, by which living spermatozoa are stained pink, and dead ones bluish-purple. Motility, she said, is not necessarily a measure of viability. Mrs. HARVEY said she has used the method, with semen incubated at 37°C. Though all motility ceased after 24 hours it was 4–5 days before all the spermatozoa took on the blue stain, though the proportion of blue-staining spermatozoa increased steadily during the period of incubation. Dr. MANN pointed out that motionless spermatozoa are not necessarily dead, and may revert to motility; and Dr. G. I. M. SWYER (London) summed up the action of the stain as differentiating the irreversibly immotile spermatozoa from those which are motile and reversibly immotile.

Mr. A. WALTON, D.SC. (Cambridge), noted that the motility centre is in the middle-piece and tail; the head takes no part in it. Dr. SWYER said that the different parts of the spermatozoa take up the stain differently, the tail dying first and taking the blue stain while the head is still pink. "They die from the tail upwards."

Blood-supply of the Testis

Dr. R. G. HARRISON (Oxford) described the blood-supply to the testis in various animals, and showed a number of beautiful X-ray photographs of animal testicular vessels injected with colloidal bismuth. In most of those examined the testicular artery was a single vessel which formed a number of convolutions before reaching the testis. The wallaby, man, and the pilot whale offer exceptions to this usual arrangement. In the wallaby the artery, instead of convoluting, divides into a sheaf of small vessels which later unite into one vessel supplying the testis; and the veins form a pampiniform plexus which collects up into four vessels. In the pilot whale there are no convolutions and no splitting—the artery plunging straight into the testis before it breaks up. In man the artery runs almost straight, giving off branches to the cord and epididymis, and then divides into two branches, one to the lateral and one to the posterior border, which ramify over the surface of the testis, sending in, towards the mediastinum, branches which loop back on themselves. It does not, as the textbooks say, run directly into the mediastinum; and this is important since in the treatment of cryptorchidism one of the main branches may get caught up. There is some relation between arterial coiling and the fall in temperature between abdomen and testicle. In the ram the veins surround the artery, suggesting an arrangement for the exchange of heat. A rise in temperature affects fertility: when the testicles are returned to the abdomen in animals they become sterile, and the continuous application of heat to the testes is injurious to fertility. Short hot baths are probably harmless, but evidence is needed about the effect of repeated hot baths, of warm underclothing, and of such occupations as stoking.

Mr. YOUNG asked whether varicocele, which seems to be associated with subfertility, raises the testicular temperature; and other speakers discussed the effect of elastic suspensory belts often worn by athletes, especially footballers. Dr. MARGARET HADLEY JACKSON (Exeter) remarked on the large number of footballers among husbands of women attending the Exeter subfertility clinic; and Dr. R. G. CROSS (Dublin) hinted that the British are supposed to be sterilising themselves by hot-bathing, and the Americans by wearing warm tight pants. It is time, he said, that we paid some attention to the kilted races.

Mr. SNAITH said that there is no evidence of correlation between varicocele and subfertility; but patients believe that there is, and they need reassuring. Dr. WALTON mentioned that the largest varicocele he has ever seen was in a very fertile ram. Dr. W. J. TINDALL noted that the chemical output of the gonads is affected by temperature: if they are transplanted to the ears the output of hormones is increased.

Uterotubal Insufflations

A paper by Mr. ALBERT SHARMAN, M.R.C.O.G. (Glasgow), was read in his absence by Miss M. MOORE WHITE, F.R.C.S. (London). He reminded the meeting of the importance of using carbon dioxide rather than air or oxygen for the Rubin insufflation test, and said that he has not encountered any ill effects from using a pressure of 250 mm. Hg as a routine. Tubal spasm is a common cause of negative findings, and he has found that only 32% of cases showing non-patency in a single test have occluded tubes. If, after a negative result, the cervix is dilated and a second insufflation is done, the spasm may be resolved. Insufflation, or even dilatation alone, may be followed by pregnancy, and this result is attributed by Rubin to the establishment of patency, removal of the cervical mucous plug, or dilatation of the tubes, or possibly to a psychic effect. Mr. Sharman believes that the addition of a kymograph to the insufflation apparatus makes it possible to distingush between tubes which are normally patent and those which are the site of spasm, stenosis, or adhesions round the tube.

Dr. JACKSON said that it is often possible to differentiate spasm from stenosis by the type of pain felt at

Digitized by Google

insufflation. Central abdominal pain associated with a tracing of the occlusion type generally means spasm, while pain—often milder—in the iliac fossa or at the back means occlusion. Dr. SWYER said that Newman had not been able to confirm Rubin's claim that the pressure waves in the kymogram derive from the tube, and Miss MOORE WHITE stated that after removal of all but 1 in. of tube on one side, and all but $1^1/_2$ in. on the other, she has still seen peristaltic waves in the kymogram, which could hardly have originated in the tubes. Mr. SNAITH would not hesitate to do a Rubin's test on account of transitory inflammation of the cervix—except perhaps in the case of gonococcal cervicitis. Dr. JACKSON and Miss MOORE WHITE mentioned that repeated patency tests must be done before the tubes are regarded as occluded; and Dr. Jackson emphasised that use of the volsellum on the cervix may send the tubes into spasm. The cervix should be handled gently.

Hysterosalpingography

Miss JOSEPHINE BARNES, F.R.C.S. (London), described hysterosalpingography with water-soluble radio-opaque media. Iodised oil, she said, is not absorbed from the tubes or peritoneum; if it becomes inspissated in the tubes it may conceivably cause stricture, while iodised-oil granulomata have been known to form in the peritoneum. Kjellberg, in a monograph on *Hystero-salpingo-pelvigraphie*, describes the use of diodone injection ('Perabrodil') which, he claims, injected in dilute solution, outlines the pelvic organs and makes possible the diagnosis of ovarian tumours and some other lesions. Miss Barnes uses a watery solution of diodone. A viscous solution has been tried but caused severe pain. The lack of viscosity is not a serious drawback, however, and the watery solution does not cause spasm. An instantaneous radiogram is taken at the very moment when the fluid is injected, and 20 minutes later another is taken off the whole abdomen. The first shows the fluid taken up rapidly into the tubes, and demonstrates any blockage; the other shows excretion of dye already beginning in the kidneys. The whole procedure is complete in about half an hour.

Dr. ERNST FRIEDMANN (London) said that he had used 'Viscyazol' in nearly 50 cases without ill effects or complaint from patients. This preparation, which is 50% diodone, will shortly be on the market in this country.

Sims Test and Male Infertility

Miss GERTRUDE DEARNLEY, F.R.C.O.G., reviewed briefly the development of the subfertility clinic at the Royal Free Hospital, London. It was begun in her department by Miss Moore White in 1937, and now carries seven doctors and a part-time registrar.

Dr. MARY BARTON (London) said that she chose to do the Sims test in the late follicular or ovulatory phase, taking mucus from the upper as well as the lower portion of the cervical canal. The normal picture 24 hours after intercourse is of mucus densely invaded by spermatozoa, many showing rapid movement. This picture rules out serious oligozoospermia and asthenozoospermia, but not some other forms of male infecundity. The cervical mucus allows only strong and well-differentiated spermatozoa to pass—apart from a few lively forms, like microsperm. She noted that the head of the spermatozoon changes, when it enters the mucus, from spatulate to olive-shape. A positive Sims test may mask pyospermia, since polymorphs in the semen do not penetrate the mucus; nor does the test reveal exfoliative conditions of the testis. A couple may give repeated positive Sims tests without conception taking place, even when no other recognisable infertility factors are present, yet conception may occur after a focus causing pyospermia has been eliminated. For this and other reasons the Sims test should be supplemented by semen analysis. Spermatozoa may be found in the fornix in reasonable quantities when none are found in the cervical mucus; this does not imply male infecundity, however, since the mucus may be specially resistant to invasion. This finding should therefore always be followed by a cross-invasion test, the husband's semen being tested against the cervical mucus of another woman, and the wife's mucus against the sperm of another man. Sometimes the spermatozoa invade the test mucus, and conversely the wife's mucus may admit the strange spermatozoa. Such incompatibility is not necessarily permanent. In other cases, though the husband's spermatozoa invade the wife's mucus they quickly become immotile. Cervical mucus contains reducing substances which may be used to nourish the spermatozoa; and possibly the supply may be insufficient to meet the needs of a dense invasion. The Sims test may also reveal a curious condition in which no spermatozoa at all are found in the cervix or vagina, even though the semen obtained by masturbation is rich in them, and can be used successfully for artificial insemination.

Testicular Biopsies

Dr. FRIEDMANN discussed the technique of testicular biopsy. He takes the specimen with the patient under gas, and uses the type of instrument designed for liver biopsy. The specimens give valuable information about the state of the seminiferous tubules, and repeated biopsies can be used to check progress under treatment.

Testosterone Implants

Miss MOORE WHITE reported on the results of a series of testosterone implants made by Mr. George Qvist at the Royal Free Hospital. He implanted 200 mg. of testosterone, and in a few cases the semen showed improvement, but results on the whole were not encouraging. In one couple who did not report back the wife conceived and miscarried; no others conceived. Biopsies might have shown that some of these cases were unsuitable for implants, and in future it is hoped to do biopsies as a routine.

Vitamin E

Mr. NORMAN WARREN (London) had given vitamin E to 50 cases of oligospermia in doses of 30 mg. twice daily; semen analyses were done beforehand. There was an increase of density of spermatozoa in 23 cases, in 18 an improvement in motility and viability, and in 17 an increase in volume of semen of more than 0·5 ml.; and a lower percentage of abnormal forms was found in all cases where there was improvement in any of the other three factors. He concluded that this group showed some response to vitamin-E therapy.

Dr. H. A. DAVIDSON had treated 42 subfertile patients over twelve weeks with 'Ephynal' tablets, 10–14 mg. daily; 12 received methyl testosterone in addition. In 29 cases there were normal variations only; 6 showed some improvement, and 7 some deterioration. Two pregnancies were reported, one of which ended in abortion. Comparable results, he said, could have been found in a similar group receiving no treatment. Lest synthetic vitamin E is less effective than the natural product he proposes to treat a similar group on wheat-germ oil.

Dr. JACKSON had treated 50 subfertile men over periods ranging from three weeks to two years with 'Fertilol,' 'Viteolin,' or ephynal capsules in dosage roughly comparable to that of Dr. Davidson. Half of them received some other treatment as well. Some had large numbers of specimens examined and 35 had at least three such examinations; so it should have been possible to demonstrate any improvement. There was little evidence that vitamin E had any effect, good or bad, and most of the variations could be matched among men who had received no treatment. Of the wives,

Digitized by Google

14 (28%) conceived, which does not compare favourably with 33% of conceptions among 324 wives attending the clinic during the same two years. She concluded that though there is little evidence that spermatogenesis can be improved by vitamin E, it is possible this vitamin may prevent further degeneration in an already damaged testis.

Basal Temperature Charts

Dr. JACKSON said that the morning rectal temperature chart helps the doctor to sort out irregular cycles, to prognosticate the day of menstruation, and to diagnose pregnancy, sometimes in advance of a report on the Aschheim-Zondek test. Persistence of the high "luteal" temperature beyond fourteen days strongly suggests pregnancy. In 2 cases she has been misled: both patients were obsessionally anxious for a child and induced a state of phantom pregnancy. Their periods were inhibited for some months; their rectal temperatures were raised, and they insisted on remaining in bed for weeks. The temperature did not fall until they were made to get up and go about their business. Such cases, however, are rare.

Impotence and Fertility

In the general discussion on the foregoing group of papers, Dr. DOROTHY TAYLOR asked for advice on the treatment of partial impotence. Miss MOORE WHITE said that successful artificial insemination of the wife with the husband's semen often resulted in the husband's recovery from impotence. Dr. DAVIDSON mentioned a syringe which he and Dr. Joan Malleson had devised for taking up the semen from nocturnal emissions, for the artificial insemination of the wife; the number of emissions can be increased by giving testosterone. Dr. JACKSON had found one husband who recovered on being directed to do so by the doctor, while Dr. JOHN HOLT (Holland) finds a successful method is to forbid the husband to have intercourse with his wife.

Dr. A. C. CROOKE (Cambridge) said that one group of steroids, which includes testosterone, is androgenic, while another group is spermatogenic. He has had promising results in 3 out of 4 cases treated with androstenediol dipropionate, which he synthesises himself.

Miscarriage Related to Seminal Characteristics

Mrs. HARVEY discussed the relation of seminal characteristics, especially oligospermia and high numbers of abnormal spermatozoa, to abnormal development of the fœtus resulting in miscarriage or stillbirth. Her figures refer to a group of over 700 husbands attending the Exeter subfertility clinic who were responsible for 745 conceptions ending as follows: 409 live births with 15 neonatal deaths, 261 spontaneous miscarriages, 24 stillbirths, 5 ectopic pregnancies, 2 induced abortions, 27 pregnancies still in progress, and 17 doubtful early conceptions. Moreover, 371 wives have had no known conceptions. She showed that the number of spermatozoa, and their motility and morphology, but not their viability, are correlated with the chance of conception. There is little evidence that any single factor in semen conduces to miscarriage or stillbirth; but the miscarriage-rate, contrary to expectation, is highest among the wives of men in the 3A group [1]; which implies that the maximum chance of miscarriage is associated with a density of 40–59 million sperm per ml., and falls off on either side of this range.

Assessment of Infertility Data

Dr. SWYER gave a survey of papers on infertility published in four American and two British journals in 1946–47 to show how exceedingly inaccurate, and even unscrupulous, authors sometimes are in the presentation of their papers. In the subsequent discussion editors were criticised for publishing such misleading work.

1. Harvey, C., Jackson, M. H. *Lancet*, 1945, ii, 99, 134.

PNEUMOCONIOSIS

SOME FURTHER COMMUNICATIONS

AT the International Congress on Industrial Medicine, which we reported briefly last week, four whole sessions were devoted to pneumoconiosis, and these deserve separate notice.

A paper by Dr. J. DANTIN-GALLEGO (Spain), entitled New Ideas on the Ætiology and Pathogenesis of Silicosis, was based on the premise that until recent times silicosis has not been studied scientifically and that no-one has yet considered the effect of the environment in the development of the disease. He thinks that too much attention has been paid to the chemical effect of silica, and that the radiographic appearances have not been correlated with the pathological anatomy. For his own part he assigns great importance to the total mineralogical constitution and physical properties of inhaled dust particles on the one hand and the human reaction on the other.

Prof. JETHRO GOUGH and Dr. J. E. WENTWORTH presented a new technique for cutting thin sections of the whole lung and mounting them on paper, a method which constitutes a distinct advance in the study of lung lesions. The focal emphysema of coalminers and trimmers is shown with great clarity, and the pathological features can be correlated with the radiographic appearances.

Dr. A. BRUUSGAARD (Norway) described some cases of pneumoconiosis in workers exposed to silicon carbide dust, which has been thought to have little effect on the lung tissues. Of 32 workers in a carborundum factory 10 showed radiographic lung changes, some of them nodular in character. In the more advanced cases there was slight disability. Most of the affected men had worked in a dusty atmosphere for more than fifteen years. (In the absence of pathological evidence it is not possible to be certain about the cause of the X-ray shadows; some might be due to deposits of carborundum, but fibrous changes might account for the incapacity found in some cases.)

Pneumoconiosis in coalminers was the subject of a number of papers. Prof. E. J. KING with Dr. C. V. HARRISON and Dr. S. C. RAY dealt with the experimental aspect, while Dr. I. DAVIES and Dr. K. J. MANN offered a classification of coalminers' pneumoconiosis based on X-ray appearances. In the South Wales area the basic X-ray abnormality consists of minute opacities, 0·5–1·5 mm. in diameter, circular in outline and varying in density. These may remain discrete or aggregate to form larger granular opacities. Two stages of pneumoconiosis, simple and complicated, are recognised. Each stage is subdivided into categories, three in the simple type and four in the complicated.

Progression of the X-ray shadows in coalminers was described by Dr. C. M. FLETCHER. Two groups were studied: in one the men had had no further exposure to coal dust after the first radiograph, and in the other they had continued to work in the mines. In the former no increase in the characteristic generalised opacities of simple pneumoconiosis was seen, whereas in the latter the opacities increased in number rather than size. In both groups, however, a majority had developed localised coalescent or massive shadows associated with a raised erythrocyte-sedimentation rate at the second examination. It is concluded that this type of progression is not dependent on continued exposure to coal dust but to an additional factor which may be infection by tuberculosis.

Prof. J. LECLERCQ, with Dr. E. BALGAIRIES, Dr. BONTÉ, and Dr. G. DECLERCQ (France) demonstrated the value of tomography in localising the masses in the pseudotumoral form of silicosis, and Dr. G. C. E. BURGER (Netherlands) discussed the efficiency of mass miniature radiography in the detection of reticulation and granulation. A practical trial with patients suffering from the earliest stages of granulation proved that, when compared with large films, the 40 mm. miniature films revealed the changes well. Studies of the electrocardiogram in silicosis by Dr. F. LAVENNE (France) showed that the most important changes were those usually associated with right ventricular hypertrophy and that they were

Digitized by Google

related not to the radiographic appearance of silicosis but to the degree of emphysema present.

Dr. W. C. DREESSEN (U.S.A.) surveyed the development and trends of studies of pneumoconiosis in the United States during the past decade. Physiological research and clinical investigations have opened up many new fields; but further basic studies are needed, since it is becoming apparent that other air-borne particulate materials besides silica and asbestos are causing serious pulmonary disease.

A neat paper by Dr. A. J. VORWALD (U.S.A.) on diatomaceous earth pneumoconiosis was memorable if only because it showed how an investigation should be made.

Diatomaceous earth is a fine-grained material composed of the siliceous residue of diatoms and other microscopic species that live in water. Clinical and experimental evidence show that both crude and fluxed calcined diatomaceous earth are capable of producing pulmonary fibrosis, the latter more than the former. Though there are scattered foci of hyalinisation and necrosis, not unlike the pulmonary response to inhaled quartz, the fibrosis is more diffuse and cellular in type and involves more especially the alveolar walls in addition to the periarterial and peribronchial tissue. The alveolar spaces are either obliterated, greatly distorted and small, or enlarged to form emphysematous areas. The diffuse cellular pulmonary fibrosis is more serious than the discrete nodular fibrosis of uncomplicated silicosis, and is perhaps responsible for the pronounced shortness of breath seen in this disease. The fused calcined product, which contains more cristobalite (a form of free silica) than the crude material, has a deleterious effect on any associated tuberculous infection. Dr. Vorwald stated that he has not yet finally identified the specific component of diatomaceous earth responsible for the observed clinical and experimental effects.

Dr. A. BRUUSGAARD and Dr. K. B. SKJELBRED-KNUDSEN (Norway) described cases of silicatosis in a talc mill, and Dr. F. BARTÁK and Dr. M. TOMEČKA (Czechoslovakia) showed that a pneumoconiosis, which they called stannosis, can develop after inhalation of the dust of tin oxide. They did not, however, make it very clear whether they regard the dust of tin oxide as noxious or inert, though they did point out its radio-opaque qualities. They also drew attention to the "euphoric state of those even gravely affected"—presumably those showing conspicuous X-ray changes—and mentioned the macrophagic but no other type of reaction in the lung tissue. (All of which suggests that the dust of tin oxide is not very harmful and that "stannosis" can be classed as one of the benign pneumoconioses, of which siderosis is the best-known example.)

The physiological aspects were discussed by, among others, Dr. TORSTEN BRUCE (Sweden) who dealt with exercise-tolerance tests and spirometry. He stressed the fact that the dyspnœa of silicosis has a physiological background and that the lungs have several mechanisms whereby they can adapt themselves to the strain produced by the destruction of air cells. In addition to chemical stimuli he mentioned the significance of the nervous regulation of both ordinary and the forced breathing in silicosis. Dr. P. PELNAR (Czechoslovakia) described a new method of examining respiratory and circulatory functions with special reference to silicosis. The method consists in continuous measuring of the oxygen and carbon-dioxide equivalents at rest, during exercise, and during recovery from exercise. In silicosis he finds that his results do not correlate well with the X-ray findings, but there is a correlation with the stage of dyspnœa and the degree of incapacity.

"Science reporting and interpretation does not accomplish its purpose . . . if it does not bring about an appreciation and a utilization of the method of science in everyday life. . . . If the great mass of the people, through accurate and interesting accounts of the successes and failures of science, can glimpse and understand that essence of science, its trying, testing, and trying again, if they build their own convictions that this is a good, sensible, successful, and useful method, then there is hope that they will apply it more widely to everyday life, to our human relations, to running our businesses, to our governments, to everything that we do."—WATSON DAVIS, *Science*, Sept. 3, 1948, p. 241.

THE NEW ZEALAND HEALTH SERVICE

FROM OUR CORRESPONDENT

THE report of the Medical Services Committee has been tabled in the House, and discussed in the press, but not so far by profession or parliament. The committee was composed of four members from the British Medical Association, and three (two medical) from the health department, with a legal chairman. Its object was to advise the government about the present medical scheme, which has been seven years in operation, and to suggest ways and means of overcoming admitted abuses. It thus represents the first major effort to overhaul the system; but it does not deal with many large aspects such as hospital reform, nursing, medical education, and the health department.

Administration.—Committees for continuous advice in policy, discipline, and ethics are proposed for the first time, the onus to be placed largely on the medical men.

General-practitioner Services.—The present fee-for-service scheme is to be retained, a number of minor adjustments and simplifications being recommended. The report debates capitation, salaries, and combinations of these, but for various reasons finds them unacceptable.

Specialist Services.—These represent the only major gap remaining in the New Zealand scheme. The report proposes a fee-for-service system, an extension of "open" (part-time) hospital appointments to help to attain the greater number of specialists alleged to be required, and the construction of a roll of acknowledged specialists based on higher qualifications, experience, &c. Many details are left for negotiation.

Pharmaceutical Benefits.—Reasons for soaring costs are examined, and the imposition of a partial payment on the patient is proposed.

It will be interesting to observe the reception given to these proposals by parliament and profession, and what, if anything, will be done. The difficulty of such piecemeal repair work is obvious to anyone who takes a broad view of the whole system of health services. There never has been any attempt to synthesise and coördinate plans for the whole; and until this is done, essentially to the satisfaction of the parties concerned, there is little prospect of progress.

MEDICAL DEFENCE UNION

AT the annual general meeting, held in London on Tuesday, Mr. St. J. D. Buxton, the president, recalled that last December the union decided to admit dental practitioners to membership and to provide advice, indemnification, and protection for practitioners overseas. He warned members to consult the secretary as soon as they find themselves in any medicolegal difficulty, for successful defence is often prejudiced by action taken before seeking advice. During the year, he said, the union had conducted nearly 1600 cases, a rise of 14% on 1946. Previously the highest annual figure for indemnity and law expenses was about £21,000; but "this year we have already committed ourselves to a sum in excess of £40,000 and there remain more cases to be settled or fought in the courts." Of the annual subscription, still at £1, over 13*s*. went in law charges and indemnity claims.

The annual report shows that, with 32,075 members on July 20, 1948, the deficit was £1344 on last year's working. One case cost it £15,791, the member having paid £10 in subscriptions. The total funds available, inclusive of the guarantee fund, amount to £189,736.

Referring to the 49 cases of alleged negligence dealt with, the report discusses the trend of judicial opinion and says that it is becoming easier for claimants to succeed in any class of action arising out of insurable risks—e.g., traffic and workmen's compensation cases. "Therefore, the tipping of the scales in favour of plaintiffs in cases in which the union is involved is only part of a larger whole." Though the doctrine of *res ipsa loquitur* has not yet been wholly applied to a case involving medical negligence, some recent cases have come close to casting on the defendant the burden of proof that negligence was absent. Certainly, the courts have felt justified in accepting as proof of negligence evidence which would not have satisfied them before the war. Probably (the report suggests) this leniency is only temporary, and judges may presently recognise that the pendulum has swung too far.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

A FRIGHTENED young man of six met me in the duty room that night. I was told he had swallowed some berries, so for once having thoroughly read my journals, I seized a tube and washed him out. That sounds easy, but I have had difficulty in penning this, for my index finger has still not recovered from the bite he gave me. By now he had fixed dilated pupils. *Atropa belladonna*, thought I, until I saw green berries. I called a colleague. Of course, when he got there the boy's eyes were normal, his adrenalous fear having passed.

By this time the boy had recovered from his treatment, and (I feel with malice) stated that his playmate had eaten more than he had. But we were loth to wash out more stomachs until we knew what the berries were. So two porters and I, very shady-looking characters all, trailed the boy's parents through hosts of doctors, all of the same name and all very sleepy, and finally got a description of the berry-bearing area. Armed with a torch, and keeping a wary lookout for the copper on his beat, I scaled the fence of the park, and crept like a felon through scrub and semi-desert until I found a good strong growth of berried weed in the place described. Tearing off a large portion of bush, I returned to the hospital. There, with the aid of the *Lancet* for Sept. 11 and one forlorn berry on a large mass of vegetation, we identified *Solanum dulcamara*, or Woody Nightshade.

While the radio blared "Woody Woodpecker," we waited for the boy's pal, a wee thing of 4, to get to the hospital. As soon as she arrived I again passed the tube. It blocked. So my colleague, asking her to open her mouth, tickled her tonsils with a spoon. She vomited. He told her it was not enough. So she obligingly vomited again. He then said "Open wide," and made her sick again. A much better method, thought I, massaging my finger.

My colleague now rang up a toxicologist of repute to ask him for an antidote. "An antidote?" quoth he. "What a question to ask me. I only know what killed 'em, not why they got better." A pleasant outlook . . .

As the nursing staff had only kept the non-berry-bearing residue, I finished the evening's entertainment by sorting through the whole dirty linen of the ward for twelve hours (3 incontinents!), to find at last a berry from the boy's stomach. If this proves anything, it is my pet theory that children love to be made sick. What else can swings, roundabouts, and synthetic sweets do to make them feel and look so happy?

Please, dear *Lancet*, continue to publish accounts of rarities just a week before I need them.

* * *

In the present emergency, a number of practitioners have approached me for notes on the plastic surgery of the cigarette, and these I now give (I'm sure the Medical Research Council won't mind).

Dislocation, due to sale without the usual container, is readily reduced by running through the fingers several times.

Fracture is invariably compound, and occasionally comminuted. Neither plaster nor Unna's paste should be used as occlusive dressings. Collodion is all right if you don't mind the smell of shoeing horses. The treatment of election is recapsulation by the method described under plastic reconstruction (below).

Herniation of the contents at both ends is incurable, though in early cases I always put it back with an eye spud.

Plastic reconstruction by the Wandsworth-Dartmoor technique is rapidly gaining popularity even in Harley Street; the opportunities for it, in general practice, can be supplemented by putting out more ashtrays in the waiting-room and looking underneath the grate in the rooms to which patients have access. Messrs. Fiddle and Flog of New Ravenish St. will shortly advertise a portable steriliser for the squeamish, and the operation should then become a routine procedure throughout the profession. In its simplest form, it is undertaken by selecting a suitable former, of a diameter slightly greater than that of your own or your patient's favourite brand. Old metal catheters matched to the size of a Weight, a Player, and a Churchman's No. 1 make a suitable armamentarium, or a convenient set may be turned up from aluminium rod. A suitable capsule is rolled on this, the length of the implants is carefully adjusted to provide a clean surface at each end, and the former withdrawn in stages, being replaced by the implants, which are slightly reduced in diameter by rolling between finger and thumb. This operation may with practice be conducted in the privacy of the pocket. A single strand of fine surgical wire passed longitudinally down the middle of the finished article protects the operator's clothes from any possible fire hazard during consumption.

Exsanguination-transfusion, with dilution of the contents, rarely meets with success, practical or social. Some workers, who must have impaired powers of olfaction, recommend as a diluent:

℞ Tussilag. fol. exsicc.
Rubi fol.
Lavand. flor.
Trifolii flor. aa part. aeq.
M. Trit. secundum artem.

I don't use any of these techniques myself. I once saved all fifteen of my tobacconist's kids from dying of external auditory meatitis—I should worry.

* * *

I must warn my fellow peripatetic who wrote lightheartedly about patterned American neckties that in at least one city of the United States (Omaha, to be precise) he is probably a marked man. He certainly has injured the feelings of the mayor of that ancient and delightful city. According to the *New Yorker* his Honour has a ruling passion and that is neckties. He has in fact carried unique distinction as a tie-fancier. Having started collecting them at the age of 18, by February of this year he had collected some 1900 ties. This number has no doubt increased since then, for whenever he or his scouts see a new pattern he does not rest until he owns it. All he asks is that it shall be sufficiently colourful and capable of filling up the shirt bosom. He has paid as much as 35 dollars for an exclusive design. How exclusive they can be may be judged from the fact that one tie carries a portrait of his Honour himself while another features a hand-painted picture of a lady ice-skating star. The most exclusive, however, must be one made of the skin of an unborn calf presented to him by a Texan cowboy. He has one made of doe-skin and several of leather; though, as might be expected, the bulk are of silk.

All this is set down to impress on my fellow correspondent that he must keep away from Omaha. Unless, of course, he goes in his yellow waistcoat and bearing some very special gift to propitiate the mayor—a strip from one of Picasso's pictures; or (perhaps cheaper) a nice logarithmic phonocardiogram in glorious Technicolor.

* * *

I recently acquired a practice; so the local insurance committee, as was the custom, circulated a notice to all the panel patients informing them of the change of doctor. However, owing no doubt to recent world events, the insurance records are not always up to date, as the following letter shows.

Dear Dr.—The person on the form sent in was my father, and he died April, 1940, so I don't think he needs any attention from anybody.—Yours truly, Mrs. —.

* * *

Nearly three months has passed since the fateful day and the world goes on. Patients recover, patients die, babies are born, and we are still here. To be sure Mrs. Jones has cast aside great-aunt Mary's old glasses and is the proud possessor of a pair of her own "made to measure," and Mrs. Smith, who has found her mother's discarded dentures are all very well for weddings, funerals, and such like festivities, though of course not for eating, is beginning to have doubts about whether naked gums are the best implements for tackling our post-war food, now that you can get new teeth free "on the panel." But apart from a decided increase in my ink expenditure there is little change. The roaring torrent of E.C.40 has changed to a modest trickle and up to now life isn't so bad. I've given up scanning the advertisements for a new line in belts: "small size with extra notches, allowing for further reduction, especially designed for the medical profession." Perhaps they won't be necessary after all.

Digitized by Google

Letters to the Editor

ACCIDENTAL INTRA-ARTERIAL INJECTION OF DRUGS

SIR,—May I make some comments on Mr. Sol. Cohen's paper of Sept. 4 and 11 ?

He begins with the assumption that the phenomena he describes are due to intra-arterial injections, which cause vascular damage and thromboses, but he does not show that all the injections actually occurred by this route. In a high proportion of cases no evidence of intra-arterial injection could be found at operation. The fact that arterial thromboses developed in some of them is no proof that the drug was injected into an artery. Indeed, there is much evidence that Mr. Cohen's assumptions are unjustified :

1. According to several authors he quotes, thiopentone has been injected into arteries without pain or other ill effects.

2. With thiopentone the symptoms began with local or peripheral pain immediately on beginning the injection; but thrombi take time to form.

3. In some of the cases there were no changes in blood-pressure, and no clinical signs of arterial or venous obstruction, and at operation thromboses were not found in the blood-vessels (e.g., case 7). In fact, the radial pulse may be full, as in case 3. The same is true of the case of gangrene following 'Myanesin' injection which he mentions.

4. On his own showing, the initial symptoms in the thiopentone mishaps are completely relieved by sympathetic nerve block, which indicates that they cannot be due to irreversible pathological changes in the blood-vessels, such as thromboses.

5. In the thiopentone cases, the pain which comes on immediately after injection may be followed by vasodilatation on one side, or in the whole of the hand and forearm, or by a white hand and cyanosed fingers. These are the signs of excessive arteriolar vasoconstriction. The vascular and other changes were relieved by sympathetic block, indicating that they originated in changes in the activity of vasomotor nerves. One patient later developed Raynaud's phenomena, which may result from purely neurological lesions, such as syringomyelia. Two patients developed severe generalised vasomotor reactions and poor pulse in the opposite limb. These are the effects of alterations in the activity in vasomotor nerves.

6. In the affected limb, in addition to the pain, there later appear muscle spasm and sensory disturbances, such as tingling, a sensation like a tight band round the limb or that the arm is being broken, vascular changes, œdema, blisters, and punctured sloughing sores. In case 1 the hand and forearm were completely anæsthetic and the hand tingled. In case 3 the entire hand and ulnar aspect of the forearm were anæsthetic, and extension, pronation, and supination movements were impossible. In case 5 there was complete loss of voluntary movement of the wrists and fingers, but passive movements were possible and painless; case 8 showed "glove" anæsthesia. In cases 4 and 8 anæsthesia and atrophy of the intrinsic muscles of the hand appeared, and in two cases carpopedal spasm. All these symptoms are familiar to neurologists and are identical with those resulting from irritation of peripheral nerves—e.g., in brachial neuritis and causalgia—and with the initial effects of injection of 'Proctocaine' into a nerve.

In Schmuttermayer's case quinine was injected into the upper arm producing the signs of a radial nerve palsy; but Mr. Cohen states that this also caused symptoms suggestive of intra-arterial injections.

All these facts suggest that the author is confounding the effects of intraneural and intra-arterial injection. That the effect of thiopentone is primarily on the nerve cells and fibres is also shown by its very use as an anæsthetic and by the following case under my care:

A miner, aged 42, had a thiopentone injection into the left arm for a hernia operation. During the injection he had some pain in the upper arm and shoulder, and after this he developed pains in the whole limb, with some tingling, and the signs of a brachial neuritis, resulting in marked weakness and wasting of the deltoid, spinati, rhomboids, and upper-arm muscles, winging of the scapula, and weakness of the trapezius muscle causing the shoulder to drop on this side. A glove anæsthesia was present, but the pulse-pressure and blood-pressure were normal and equal on the two sides of the body and the symptoms gradually improved. It is difficult to explain such a case as due to arterial damage.

As Mr. Cohen says, intra-arterial injections are often painless unless the artery is covered with a network of sensory nerves. This suggests that sudden severe local pain following injection of drugs is due to their injection into the sensory nerves around the vessels or into the main nerve trunks. (The former probably occurred in case 1, in which blood was found around and in the adventitia of an artery.) Injections into nerves may produce marked peripheral vasodilatation, through liberation in the blood-vessels of acetylcholine from the vasodilator fibres in the nerves. Acetylcholine has been shown to accelerate blood-clotting, and excessive vasodilator nerve impulses may therefore eventually precipitate thromboses. It is unnecessary to imagine that thromboses in the arteries supplying the nerves of the limb are responsible for the neurological symptoms. It is much more reasonable to suppose that the arterial thromboses follow the neurological lesion.

The arterial thromboses which later occurred in some of the cases Mr. Cohen describes were no doubt important in causing the onset of gangrene. Nevertheless gangrene may occur as a trophic lesion, resulting from damage to nerve-fibres (as in tabes, leprosy, and bed-sores), without vascular lesions being present.

London, W.1. R. WYBURN-MASON.

DIETARY FAT

SIR,—Your leading article of Sept. 18 gives a fair account of our present knowledge of dietary fat. You will perhaps allow me to comment on it and on Dr. Walker's letter on p. 476 of the same issue.

Most of us will agree with Dr. Walker that it is unwarranted to define the deficiency symptoms of a nutrient, the minimum requirement of which is not yet known. However, the comparisons of our rations with the fat intake of other countries are not accurately quoted. Thus he states, on the authority of Fleisch,[1] that the daily fat intake in Switzerland during the war period was 40–50 g. A glance at the curves on p. 891 of Fleisch's paper shows that these figures held good only for the period from the end of the first quarter of 1944 until the end of the second quarter of 1945. Six months later the fat consumption went up by 50–60%. Even this summer, 3 years later, visitors could see that the Swiss public was still as eager a consumer of butter and whipped cream as the holidaymaker from Britain. It is perhaps fair to add that food rationing was introduced in Switzerland in 1942 and that light, moderate, and heavy workers obtained 600, 1200, and 1800 extra calories daily, consisting mainly of meat, cheese, and fats.

Your leading article enumerates the probable reasons underlying a craving for fat. Experience indicates that fat consumption depends more on living standards and national food habits than on geography, climate, or race. The average daily fat consumption in England rose from 99 g. per head in 1909–13 to 124 g. in 1934.[2] Similar rises occurred in other western industrial countries and also in the United States; and the fitness of the South African Bantu or of the Japanese, with a daily fat intake of 30 g. or less, will be of little help in establishing our minimum requirement.

In dealing with this problem the importance of the non-caloric functions of dietary fat have not always been sufficiently recognised. In a properly balanced diet[3] not only is the absorption of fat-soluble vitamins and of calcium and phosphorus dependent on adequate fat intake, but the fat also exerts a sparing action on many of the B vitamins. Another important relation of dietary fat to the economy of food utilisation was recently demonstrated in animals.[4] A mixed diet containing an adequate amount of fat secured extra calories for work, growth, and

1. Fleisch, A. *Schweiz. med. Wschr.* 1946, p. 889.
2. Brandt, K. *Ann. Amer. Acad. Polit. Soc.* 1943, **225**, 210.
3. Leitner, Z. A. *Med. Pr.* 1948, **219**, 215.
4. Forbes, E. B., Swift, R. W., Elliott, R. F., James, W. H. *J. Nutrit.* 1946, **31**, 203.

Digitized by Google

storage. These extra calories were not available after omission of fat from the diet although an isocaloric mixture of carbohydrates and proteins was substituted. Lack of more detailed knowledge led Burr [5] to conclude: "There are ample reasons for recommending that the fat intake be not reduced much below the normal established habits."

London, W.1. Z. A. LEITNER.

SUPERNUMERARY NIPPLES

SIR,—While performing routine release medical examinations in the R.A.F. in 1946, I noted the incidence of supernumerary nipples in all cases. I also noted, by questioning and examination of the medical records, the cases of neurotic illness. I can thus present figures, tabulated below, of both a "neurotic" and a "non-neurotic" series examined under identical conditions. I had no idea of finding a connexion between supernumerary nipples and neurosis as the two factors were observed for different ends. The two series are selected only in that all subjects had passed a medical board on entry and had not been discharged on medical grounds—i.e., those severely handicapped by neurosis do not appear. I found no supernumerary nipples among 139 W.A.A.F. personnel, but the whole milk-line was not examined in their case.

—	—	No. of men	No. and per cent. with accessory nipple
Men without obvious neurotic illness	—	643	48 (7·5%)
Men with neurotic illness at some time during their service	Downgraded on this account	24	2 (8%)
	Not downgraded on this account	40	3 (7·5%)
	Total	64	5 (8%)

My figures do not show any significant difference in the incidence of accessory nipples between the neurotic and non-neurotic members of this group.

London, W.2. GORDON HESLING.

POLYARTERITIS NODOSA

SIR,—In connexion with the statement by Dr. Tonkin and Professor Pulvertaft (Aug. 21) that more than half of the cases of polyarteritis nodosa survive for a considerable time, the following report may be of interest.

A married man, aged 36, was admitted to St. Charles' Hospital on April 12, 1946, with loss of weight, persistent pyrexia, asthenia, pain in joints, cough, and occasional small hæmoptyses. He had been subject to "rheumatic" pains, but had had no serious illnesses. Three years previously he was in another hospital on account of hæmoptysis, pyrexia, night sweats, and a "red eruption" on the legs; blood-count normal and blood-culture negative; provisional diagnosis was meningococcal septicæmia. From 1943 till April, 1946, his health was fairly satisfactory except for occasional severe attacks of pain in the joints, legs, and arms, unrelieved even by complete rest.

On admission.—Thin, pale, and wasted. Temperature 99·2° F; pulse-rate 96 per min.; blood-pressure 190/70 mm. Hg. Urine: no albumin. He complained of blood-stained sputum, and pain in knees and lower back. Cardiovascular, respiratory, digestive, and central nervous systems clinically normal. Skin normal except for a few purpuric spots on the legs.

Investigations.—X-ray examination: evidence of bronchitis at base of right lung; lumbar spine normal. Sputum: no tubercle bacilli on examination. Blood-cultures negative. Urine: microscopical examination showed an occasional leucocyte. Blood Wassermann and Kahn reactions negative. Blood proteins normal. The only positive findings were: (1) constant moderate polymorphonuclear leucocytosis, with no eosinophilia; and (2) increased blood-sedimentation rate.

Progress.—After two weeks the temperature settled to normal, but the patient still looked ill and had joint pains. The diagnosis was obscure until the discovery of small hard nodules in different parts of the body on May 1. The nodules were dermo-hypodermic and mostly on forearms and thighs. A tentative diagnosis of periarteritis nodosa was made and confirmed later by histological examination of an excised nodule, the report on which read: "Periarteritis nodosa. Chronic inflammation around and in the walls of blood-vessels, with in places numerous polymorphs, and one vessel contains a thrombus."

Unsuccessful attempts were made to demonstrate allergic and/or infective ætiological factors. However, the symptomatology suggested a chronic low-grade infection, and the patient was given empirically a course of parenteral penicillin from May 14 to 30. While this was being administered the temperature rose each day to 99–102° F, although it had been normal in the two previous weeks.

The patient's general well-being improved remarkably, and on May 24 only one small nodule on the inner surface of the right forearm could be seen. He was discharged home on June 10, and afterwards resumed his normal occupation of club steward. I heard recently that he is still well.

St. Charles' Hospital, London. A. I. SUCHETT-KAYE.

POLYTHENE TUBING IN BLOOD-TRANSFUSION

SIR,—Having read the article by Dr. Farquhar and Dr. Lewis in your issue of Aug. 14, I concluded that polythene catheters would be useful in blood-transfusion, particularly for patients requiring fairly large amounts of whole blood or packed red cells at a very slow rate. Using a needle as an introducer, I have found it possible to insert polythene catheters, of 1 mm. bore, into veins. The method is as follows:

A suitable length (about 9 in.) of polythene tubing, with an outside diameter of approximately 1·5 mm., is used. This will pass through a standard blood-taking needle (internal diameter approximately 1·75 mm.). The end of the catheter is bevelled to coincide with the bevel of the needle. Originally a side opening was also made in the catheter, but it was found that this weakened it so much as to make it difficult to introduce. The catheter is inserted into the taking needle until the bevels of needle and catheter almost coincide. Under local anæsthesia, the needle, with contained catheter, is then inserted into the vein. The catheter is now threaded through the needle for about 6 in. and the needle is withdrawn. Where possible, the needle has been introduced into a vein of the upper forearm and the catheter has been passed upwards until it is an inch or two beyond the elbow-joint.

If a tourniquet is used to produce venous distention, it should be released as soon as the needle has been inserted. Failure to do this may result in a leak at the site of the puncture when the needle is withdrawn. To expel all air blood is allowed to run down the catheter, which is then attached to the standard drip apparatus by means of a suitable cannula. This can be prepared by cutting a no. 1 needle so as to leave the shaft, approximately 1 in. long, with a smooth tapered tip. In all cases this has been found to give a firm joint that does not leak. Suitable cannulæ must be selected individually, for there appears to be considerable variation in the outside diameter of these needles. A sterile gauze dressing is applied at the site of puncture and the whole is held in position with a length of 2 in. strapping completely encircling the arm. The tubing of the apparatus is strapped to the arm in the form of a loop so as to prevent direct traction on the catheter, but the cannula connexions should be left exposed so that any leak may be easily detected. The rate of flow can be easily regulated between 20 and 120 drops per minute, while greater rates may be achieved by using positive pressure.

With this method whole-blood and packed-cell transfusions have been easily maintained at a rate of 20–30 drops per minute for periods of up to 60 hours.

Only in the first case did a transfusion stop of its own accord. A needle was used in the catheter connexion, together with a very short catheter. The patient was restless and the catheter was forced up until the needle was also in the vein. Both catheter and vein were punctured and a hæmatoma resulted. This difficulty has been overcome by the use of a longer catheter and the modified cannula already described.

In one case we have given by this method the red cells from 6 pints, and in another, 7 pints of whole blood. Splinting has been unnecessary and the drip continues to run when the patients' arms are folded. One restless patient twice got out of bed without interfering with

5. Burr, G. O., Barnes, R. H. *Physiol. Rev.* 1943, **23**, 256.

Digitized by Google

the transfusion, though a previous attempt at transfusion by the "needle technique" had failed because of this. Nevertheless, it is felt that a light splint might be used with advantage in the case of a restless or sleeping patient.

Leaking has never been observed, despite the fact that the introducing needle is much larger than the catheter. No case has shown any bruising. No phlebitis has occurred so far, and in one case the same vein was subsequently employed for transfusion by "needle technique."

Thanks are due to the medical and nursing staff of the wards in which these transfusions have been performed. Plastic catheters extruded to our specification were supplied by De La Rue Insulation Ltd., of Tynemouth, who have always been most helpful.

Royal Victoria Infirmary, Newcastle-on-Tyne. WILLIAM WALKER.

SPONTANEOUS RUPTURE OF THE RECTUM

SIR,—I was interested to see the recent reports of so-called "spontaneous ruptures of the rectum." One cannot help wondering whether such can indeed occur "out of a blue sky" or whether some previous ulceration is always present.

Recently I had a similar case in which laparotomy revealed a pelvis full of solid fæces which had escaped through a perforation about the size of a half-crown situated in the lower sigmoid colon. At operation the bowel appeared otherwise normal, and I was able to exteriorise the affected area. The patient's condition, however, was very poor from the start, and he unfortunately came to autopsy.

A careful search showed evidence of considerable diverticulitis, and the presence of marked engorgement around the perforation led us to believe that it was almost certainly the floor of a stercoral ulcer which had given way.

Ashford County Hospital, Middlesex. ROBIN BURKITT.

LETTER TO A NEPHEW

SIR,—I was a little perturbed by the views of the "affectionate uncle" in your Students' Number. I do not understand why the vocational urge to be a good doctor should be regarded as unhealthy, or why high ideals should be incompatible with being a "wise, kindly, reliable human being."

The two attributes are surely independent of each other. True, many idealists are extremely bigoted and narrow-minded; but there are others, of whom the late William Temple may be taken as an example, who are the most human of men. I am sure that if the "affectionate uncle" were to delve into his experience he would find far more neurotics and other unstable personalities among those with low ideals than those with high.

This condemnation of idealists as freaks is deplorable. Where would the drive for achievement in any walk of life be found if it were not for ideals? The world would drift through sloth and idleness to its own destruction even faster than it is drifting now. The man of ideals is just the very person of integrity to whom the distressed would turn in time of trouble. Although the idealist hitches his wagon to a star, the wheels of his wagon are none the less firmly placed upon the ground, and the skill that he has acquired in guiding them through the rough journey of life makes his advice all the more valuable in helping those who are not so successful. Idealism and realism are complementary.

I would suggest that the delightful picture that the "affectionate uncle" drew of the trusted family doctor itself demands a definite vocation. He sets an ideal in medical practice that requires from the doctor unremitting service to his patients at all times of the day and night. I believe that most men are idealists. They are loth to admit it, however, because of the unfortunate association in men's minds of idealism with narrow-minded fanaticism.

X.Y.Z.

PRIVATE PATIENTS NOT ADMITTED

SIR,—In your last issue you take exception to my letter to the *Times* of Sept. 15 in which I uphold the decision of the Minister of Health to exclude private patients from the new health centres because, in my opinion, this is bound to lead to either preferential, more considerate, or better treatment for them. You say—

> "The truth seems to be that the great majority of patients remaining as private patients do so in order that they may suit their own convenience as to when, where, and how often, they consult their doctor."

But surely if private patients coming to the health centre are permitted to "suit their convenience" as to when they see their doctor, whereas other patients, except emergencies, have to make appointments between certain hours, they are receiving preferential treatment, and here of course I am using the term treatment to imply service and not medical treatment for disease.

It is quite permissible to argue that to admit private patients to health centres might have compensating advantages to the doctor or even to the service as a whole by saving the doctor's time, but to deny that it would involve two standards is absurd.

London, S.W.1. SOMERVILLE HASTINGS.

SELECTION OF TEACHERS

SIR,—Your Students' Number (Aug. 28) contained a concerted attack on the problem of selecting medical students. A scarcely less important problem is the selection of clinical teachers. The present system is very inefficient—so many teachers are dull and incompetent, so few brilliant and inspiring. Your peripatetic correspondent's son (Sept. 11) might be quoted.

I do not know how teachers are selected, but it seems that teaching ability is rarely considered. For those who have to make the choice it is indeed very difficult to assess; yet they never take the obvious step and ask students. Only his audience can judge whether a teacher is lucid and capable of holding its interest. Surely, Sir, there is some way of fairly estimating a man's ability to teach by asking those whom he has taught? This should apply as much to the promotion of a registrar to a chief assistant's post as to the appointment of an honorary at a teaching hospital. It is true that there are not enough good teachers to go round, but part of the reason is that many potentially good ones stop teaching when they have finished as registrars. If medical school authorities could judge which of the registrars were able teachers, they could encourage them to continue to teach. Provided their clinical and scientific ability was sufficient, an improvement in the general standard of teaching should result.

CLINICAL STUDENT.

THE CASSEL HOSPITAL

SIR,—May I make two corrections to your account last week of the procedure used in selecting nurses for the Cassel Hospital for Functional Nervous Disorders?

Your heading described "The Cassel" as a mental hospital; it is a hospital for neurosis and it has never been a mental hospital nor admitted psychotic patients. The point is important in so far as your note may affect our recruitment of State-registered nurses for the year's course and certificate in the nursing of neurosis, or may discourage applicants for the Cassel bursaries, which permit a general trained nurse to obtain three months' intensive experience in this work, and then to return to her own hospital.

Secondly, Dr. C. H. Rogerson, my predecessor, is innocent of responsibility for the procedure, which owes much to War Office Selection Board methods. The system was introduced by the Matron, Miss D. Weddell, with the technical assistance of myself and my colleagues.

The Cassel Hospital, Ham Common, Richmond, Surrey. T. F. MAIN Medical Director.

". . . The great epidemic diseases are seven in number, malaria, plague, cholera, smallpox, typhus, yellow fever, and influenza. Others have had episodes of widespread activity, but these seven have been the great killers. . . ."—Dr. F. M. BURNET, F.R.S., *Med. J. Aust.* Sept. 11, 1948, p. 283.

Digitized by Google

Parliament

Army Cadets' Deaths from Heat-stroke

A STATEMENT circulated by Mr. EMANUEL SHINWELL, Secretary of State for War, includes the following information about the death from heat-stroke of two officer cadets at Aldershot after a physical-training exercise held on July 26, 1948.

The exercise was the fourth of a graduated series of physical-endurance exercises which formed a normal part of a physical-training syllabus designed, among other things, to make the cadets physically tough. Exercises of this type (though more severe) were introduced in 1942. They were made somewhat less exacting in 1944 and again in 1946, the latter change being the result of a fatality somewhat similar to this one. No other fatality has been reported during the last six years.

The exercises have been carried out in the past in all sorts of weather. The heat on this occasion, though exceptional, should not, taken by itself, have justified any major modification. Certain factors, however, combined to make the other conditions unusual. A strenuous morning's work, which took longer than was expected, was followed by a late lunch. The exercise was delayed and one instructor only—instead of two—could be made available.

The exercise started shortly after 3 P.M. The instructor, a sergeant, led the troop. After six miles they became somewhat strung out, and the instructor, hearing that one officer cadet had collapsed, called a halt; but, being informed that assistance had been summoned from barracks, he continued the exercise. An ambulance was summoned by telephone, but by an unfortunate chance was deflected to deal with another accident, and by the time it picked up the officer cadet some 35 or 40 minutes had elapsed. In the meantime a second officer cadet had collapsed. Cadets who were with him summoned help, and he was also collected by ambulance. Both cadets died the following morning, the cause of death being heart-failure due to heat-stroke.

"I am satisfied," Mr. Shinwell said, "that no officer or man can be charged with culpable negligence. It has been my object, however, to see that the instructing staffs at these schools should be specially picked and should realise that they have a special and important relationship to the young men in their care. I came to the conclusion that certain officers who were directly responsible for the exercise showed lack of judgment in allowing the exercise to proceed in the afternoon of such a hot day, after a strenuous morning and a rushed midday meal, and without the proper complement of instructors. I have accordingly ordered that they shall be replaced in their appointments."

A third officer cadet died after an exercise at Ripon.

The exercise was one of the standard physical-efficiency tests which are carried out once a year by all officers and men of Service units who are under 35 years of age and physically fit. This cadet had been passed medically fit for all duties on June 19.

July 28 was an unusually hot day, and in view of the heat the officer commanding the officer cadet squadron to which he belonged ordered that the officer-in-charge of the test was to take it easy and not to force the pace at all or allow the men to try to complete the course ahead of time. Also because of the heat the cadets were allowed to carry or wear steel helmets as they wished. The cadets had had an easy morning, chiefly lectures, and were not at all rushed.

The party undergoing the test consisted of about 40 cadets under an officer, assisted by a physical-training instructor and one sapper who was under training to become an instructor. The party marched for the first 5 or 6 miles; after this the officer-in-charge thought that a number of cadets would not finish the course in the time allotted, and allowed them to fall out and follow independently or to make their own way back to camp. Two cadets were sent back to the camp by car, and on arrival there an ambulance was sent to collect those who had fallen out.

Meanwhile, after about 8 miles, this officer cadet, who was among those who were straggling behind, became very distressed and collapsed. He was left under the charge of the instructor, who took him by ambulance to the camp reception station, where he arrived 45 minutes later. The medical officer-in-charge decided that the only course was to get him to York Military Hospital as quickly as possible. Emergency treatment was begun at once and was continued by the medical officer in the ambulance all the way to York, where he arrived at 6 P.M., some two hours after he had collapsed. He died of heat-stroke shortly after midnight.

Mr. Shinwell concluded that "no-one was to blame for the tragic death of this officer cadet."

Adjournment

On Sept. 24 Parliament adjourned until Monday, Oct. 25.

QUESTION TIME

The Common Cold

Mr. JOHN LEWIS asked the Lord President of the Council to what extent the Medical Research Council and other similar organisations had been concerned during the past year with investigation into the cause and cure of the common cold; what sums had been expended on this research; and what results had been attained.—Mr. HERBERT MORRISON replied: The Medical Research Council, with the coöperation of the Ministry of Health, have continued to maintain research into the nature and transmission of the infection, using human volunteers, at the Harvard Hospital, Salisbury. The cost to the council during the last financial year was approximately £9500, exclusive of hospital accommodation and services provided by the Ministry of Health. Useful progress has been made, but there are as yet no results capable of practical application. Mr. LEWIS: Is not a totally inadequate sum being spent on investigation into this matter, which quite obviously is costing the nation many millions of pounds every year?—Mr. MORRISON: If I was quite sure that by going to the Treasury and asking for a substantial addition we would automatically solve the problem, I would do so; and I agree that it would pay. But money spent upon research must be governed by the likely practical results from the expenditure. We are doing all we can. Mr. LEWIS: How can one possibly say what the likely results will be unless money is spent on research?—Mr. MORRISON: That is a very wasteful philosophy.

World Health Assembly and Mental Health

Mr. FRANCIS NOEL-BAKER asked the Minister of Health whether he was satisfied that the composition of the British delegation to the World Health Assembly was such as to enable it to play an adequate part in discussions relating to psychiatry and mental health; and whether he would consider strengthening British delegations to future meetings of the organisation by the inclusion of experts in these subjects.—Mr. ANEURIN BEVAN replied: This assembly was little concerned with technical discussion of psychiatry and mental health. I shall certainly have in mind including an expert in these subjects in any future delegations where I am clear the probable subject matter warrants it.

Compensation on Resignation from N.H.S.

Sir ERNEST GRAHAM-LITTLE asked the Minister whether in the event of a doctor electing to resign from the National Health Service shortly after entry, and having given the necessary three months' notice of resignation, his compensation for loss of practice goodwill will be payable; and within what waiting period.—Mr. BEVAN replied: Payment will be made as soon as the information is available on which the amount due can be calculated. Meantime, a payment on account will be made if hardship would otherwise be involved.

Apparatus for Cancer Research

Air Commodore A. V. HARVEY asked the Chancellor of the Exchequer if he was satisfied that sufficient U.S. currency had been made available to enable modern equipment to be purchased for the treatment of cancer.—Mr. GLENVIL HALL replied: It has been agreed with the British Empire Cancer Campaign that dollar exchange will be made available for the purchase of any scientific apparatus essential for cancer research which can only be obtained from the United States. Air Commodore HARVEY: Is the Minister aware that there is a feeling in the medical profession that for much equipment which is required dollars are not available, and if these requests are made to the Bank of England will he instruct the Bank to deal with these applications favourably?—Mr. HALL: My information is that everything is working very smoothly. We have had no complaints whatever.

Digitized by Google

In all cases where application has been made, dollars have been forthcoming.

Mr. F. J. ERROL: As the Member referred only to equipment for cancer research, does his reply, therefore, imply that no dollars are to be available for the purchase of equipment for cancer treatment as opposed to cancer research?—Mr. HALL: As to treatment, no application has been made. If an application is made, dollars will be found.

Extra Food for Blood Donors

Dr. LOUIS COMYNS asked the Minister of Food if he would consider the possibility of granting extra food points as an encouragement for blood donors.—Dr. EDITH SUMMERSKILL replied: Blood donors are never asked to give blood sufficiently frequently to impair their nutritional state. They are, of course, given refreshments at the blood-transfusion centres, and the Ministry of Food makes allowances of tea, sugar, milk, and biscuits to the centres.

Tuberculosis in the Navy

Replying to a question Mr. W. J. EDWARDS, parliamentary secretary to the Admiralty, gave the following figures of the incidence of tuberculosis in the Royal Navy.

Officers and Men invalided for Pulmonary Tuberculosis during the years 1940–46	9010
Cases accepted by the Ministry of Pensions during the years 1940–46	9614*
Attributable	3777
Aggravated	5837
Deaths during service	430

* Includes post-discharge claims from men invalided for reasons other than tuberculosis.

Health Benefits for Foreigners

Captain JOHN CROWDER asked the Minister whether his regulations entitled foreign nationals on a short visit to Great Britain to full benefit under the National Health Scheme, including the replacement of dentures or spectacles.—Mr. BEVAN replied: Yes.

Visitors to Ulster

Sir RONALD ROSS asked the Minister what arrangements he had made for those registered under the National Health Acts of Great Britain and Northern Ireland, respectively, when in that portion of the United Kingdom to which the Act under which they are registered does not apply.—Mr. BEVAN replied: So far as Great Britain is concerned, the benefits of the National Health Service are fully available to persons from any parts of the United Kingdom or elsewhere. As regards Northern Ireland, where the health service is provided under an Act of the parliament of Northern Ireland, I understand that arrangements have been or are being made for the service to be available to persons normally resident in Great Britain.

Health Centres

Sir HENRY MORRIS-JONES asked the Minister how many health centres had been set up under the National Health Service Act; and whether he had any plans for the establishing of further centres in populous areas.—Mr. BEVAN replied: 26 dispensaries from which general medical and dental services were provided before July 5 are continuing as health centres under the Act. I have approved a proposal to build a centre on a developing housing estate in London; and the provision of centres in other populous areas is under consideration.

Fees for Ophthalmologists

Sir ERNEST GRAHAM-LITTLE asked the Minister if he was aware that by the regulations S.I. 1273, 1948, and the statement specifying fees and charges for sight-testing opticians, the specialist ophthalmic surgeon, with at least ten years' study before undertaking practice, would be at a monetary disadvantage as compared with the optician, who had had no comparable training, as in the example submitted to him; and if he would reconsider this position.—Mr. BEVAN replied: I do not accept the assumption underlying the question. The remuneration of ophthalmic medical practitioners taking part in the supplementary eye service has been fixed, in agreement with the profession, in the light of the Spens report on the remuneration of consultants and specialists. The remuneration of opticians for the supply and fitting of glasses is approximately equal to the remuneration they received for the same services under the National Health Insurance scheme.

Cost of Prescriptions and Spectacles

Sir HENRY MORRIS-JONES asked the Minister whether he would state the estimated cost of prescriptions dispensed under the National Health Service Act, and also the cost of supplying spectacles.—Mr. BEVAN replied: The estimated cost of prescriptions dispensed from July 5 to Aug. 5 is nearly £1,500,000. The amount paid from July 5 to Aug. 31 for sight-testing and supplying glasses under the supplementary ophthalmic service was £237,433, though this figure does not represent the full liabilities incurred during the period.

Cost of Dental Treatment

Sir ERNEST GRAHAM-LITTLE asked the Minister the cost to date of dental estimates submitted or approved by the Dental Estimates Board.—Mr. BEVAN replied: The board has authorised payment of a total of £708,307 up to Sept. 17.

Artificial Insemination

Mr. T. E. DRIBERG asked the Minister what facilities for artificial insemination were provided at clinics under the National Health Service; if such facilities included both A.I.(H.) and A.I.(D.); what information he had received from such clinics regarding the physical and mental health and development of children born as a result of artificial insemination; and if he would also make inquiries on this subject from private clinics.—Mr. BEVAN replied: No such facilities are provided. On the last part of the question I am not advised that such an inquiry would be justified.

Foot Clinics

Mr. SOMERVILLE HASTINGS asked the Minister why he had decided to discourage local authorities from opening foot clinics seeing that section 28 (1) of the National Health Services Act empowered these authorities to make arrangements for the purpose of the prevention of illness and that chiropody was essentially a preventive service.—Mr. BEVAN replied: I do not want to plunge into a general chiropody service without more advice. But I have told authorities that if experience shows the need they can put in proposals to me.

Spate of Prescriptions

Sir WALDRON SMITHERS asked the Minister if he was aware that the dispensation of doctors' prescriptions had, since the introduction of the health service, increased by more than 100%; and what steps he was taking to meet this situation.—Mr. BEVAN replied: I am not aware that chemists generally are experiencing difficulty in coping with the increased volume of dispensing.

Obituary

WILLIAM FREDERIC HARVEY

C.I.E., M.A., M.B. EDIN., F.R.C.P.E.

Lieut.-Colonel Harvey, who died in Edinburgh on Sept. 11 at the age of 76, was one of the original members of the Medical Research Department in India, where he gained a solid reputation both as investigator and administrator. Soon after his retirement in 1925 he joined the staff of the research laboratory at the Royal College of Physicians of Edinburgh, and for the many remaining years of his life he went on doing valuable work, especially on the structure and classification of new growths.

Born in 1873, he spent his childhood in India, where his father was an educational missionary in Travancore State. He returned to this country to go to school at Dollar Academy, and he continued his education at Edinburgh University and University College, London. In 1897 he graduated in medicine, with first-class honours, at Edinburgh, and two years later he joined the Indian Medical Service.

The following 27 years, which he spent in India, coincided with a time of widening opportunities for research in tropical medicine, and Harvey took full advantage of them. As an officer on probation he had already met Almroth Wright, who then held the chair of bacteriology at Netley, and later while on leave he worked in Wright's laboratory at St. Mary's. He was a great admirer of Wright's method, and when appointed deputy sanitary commissioner in the Punjab in 1902 he made many improvements in the manufacture and distribution of

Digitized by Google

vaccine lymph and introduced glycerinated lymph into the province. Another lasting influence on his approach to medical problems was Karl Pearson, from whom he derived his critical approach to research.

When the government of India constituted the Medical Research Department (or Bacteriological Department as it was first called), Harvey was one of the first group of officers, which included Bannerman, Semple, Lamb, Lieut.-Colonel Glen Liston, Sir Rickard Christophers, S. P. James, and A. G. McKendrick who became his lifelong friend. His first post in the new department was as assistant director of the Pasteur Institute of India, and in 1905 he succeeded Lamb as director. McKendrick became his assistant and together they carried out the researches into the prevention of rabies which led to the introduction of Semple's carbolised vaccine.

In 1911 Harvey was appointed director of the Central Research Institute at Kasauli, where he devoted himself largely to bacteriological and immunological problems, particularly methods of technique. On these subjects he published many papers in the *Indian Journal of Medical Research*, of which he was the first editor when it was founded in 1913. His work was interrupted by the first world war; for in 1916 he was recalled to military service and appointed an A.D.M.S. in Mesopotamia. There he was one of the officers called upon to reorganise the medical side of the Army after the earlier campaigns, and his work won a mention in despatches. After an attack of paratyphoid fever he was invalided to India and he returned to Kasauli till he retired in 1925. He was appointed C.I.E. in 1921. Of this part of his career a colleague says: "Harvey was very much liked by all who came in contact with him, and his advice was freely sought and readily given on all subjects connected with research in India. He was always constructive in his criticisms of any work on which his counsel was sought."

Settling in Edinburgh, Harvey in 1927 succeeded James W. Dawson as histopathologist to the laboratory of the Royal College of Physicians of Edinburgh. The results of this new work appeared in the next 20 years in his papers in the *Edinburgh Medical Journal*, on such subjects as the standardisation of blood examination, irradiation effect on the skin, carcino-sarcoma, and chordoma. His series of studies, in collaboration with E. K. Dawson and J. R. M. Innes, on debatable tumours in human and animal pathology, were later issued as a monograph. For a short time he took Colonel McKendrick's place as superintendent of the laboratory, and he continued the heavy routine reporting involved by war conditions until 1946 when he was freed to continue his tumour studies. For his work the college awarded him the Lister and Freeland-Barbour fellowships and in 1946 the Cullen prize. He represented the college on the Imperial Cancer Research Fund committee and he was also a vice-president of the Royal Society of Edinburgh and a section editor of the *Tropical Diseases Bulletin*.

Sir Rickard Christophers writes: During his time in India Colonel Harvey played an important part in the development of the bacteriological service and especially in the expansion of the activities of the Central Research Institute, Kasauli, the government research laboratory. Not only was he an able bacteriologist and research-worker but he had high capabilities as an administrator, and many who have worked under him as director will remember his unfailing sympathetic and helpful advice and staunch support where such was needed. Though of a somewhat retiring disposition, he had a great gift of making loyal and lasting friends. He was a man of wide interests and many activities, and one of his outstanding characteristics was the thoroughness with which he carried out any work he undertook. In such cases no labour was too great and the object was pursued with a doggedness which usually achieved its end. As an example, when on retirement he became engaged in reviewing papers for a certain journal he surprised his friends by learning Dutch, and as a result must have been one of the very few British research-workers in his line who could read Dutch scientific papers in the original. After retirement and when working in the Edinburgh Pathological Diagnosis Laboratory he so developed his knowledge of tumours that he became a recognised authority on this subject. With this he was always the pleasant hospitable friend, a keen tennis-player and a great social acquisition. Many will regret his death who knew him at his station in Kasauli more as the kindly local magnate than the hard-working scientist.

Colonel Harvey married in 1910 Miss Jean Sutherland. They had a daughter and a son who is also a doctor.

Diary of the Week

OCT. 3 TO 9

Monday, 4th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. Guy Blackburn: Traumatic Injuries of the Abdomen.

Tuesday, 5th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. A. B. Wallace: Treatment of Burns.
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. R. T. Brain: Dermatoses of Childhood.

Wednesday, 6th

ROYAL COLLEGE OF SURGEONS
5 P.M. Prof. F. H. Bentley: Interpretation of Visceral Pain.
UNIVERSITY OF GLASGOW
8 P.M. (Department of Ophthalmology.) Mr. Frank Law: Physiotherapy of the Eye.

Thursday, 7th

LONDON COUNTY COUNCIL MEDICAL SOCIETY
3.45 P.M. (Friends House, Euston Road, N.W.1.) Mr. Magnus Pyke, D.SC., Miss R. M. Simmonds: Nutrition in Hospitals.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. R. M. B. MacKenna: Modern Trends in Dermatology.

Friday, 8th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. H. Jackson Burrows: Bone-graft Surgery.

Births, Marriages, and Deaths

BIRTHS

BARCLAY.—On Sept. 15, at Waltham Abbey, the wife of Mr. G. A. Barclay, F.R.C.S.—a son.
COX.—On Sept. 25, in London, the wife of Dr. A. G. C. Cox—a son.
DANCKWERTS.—On Sept. 21, at Kenilworth, the wife of Dr. Richard Danckwerts—a daughter.
EDEN.—On Sept. 16, at Vancouver, British Columbia, the wife of Dr. John Eden—a daughter.
ELMES.—On Sept. 20, at Sherborne, the wife of Dr. B. G. T. Elmes—a daughter.
GAREH.—On Sept. 20, at Harrow, the wife of Major E. Gareh, R.A.M.C.—a son.
GOWAR.—On Sept. 20, at Aberdeen, the wife of Mr. F. J. Sambrook Gowar, V.R.D., F.R.C.S.—a daughter.
HARDY.—On Sept. 18, at Truro, the wife of Dr. J. D. Hardy—a daughter.
HARMAN.—On Sept. 25, in London, the wife of Dr. J. B. Harman—a daughter.
INKSTER.—On Sept. 17, at Stockton-on-Tees, the wife of Captain J. S. Inkster, R.A.M.C.—a daughter.
KIDD.—On Sept. 14, at Grendon Underwood, Bucks, the wife of Dr. Humphry Kidd—a daughter.
LOVETT DOUST.—On Sept. 19, in London, the wife of Dr. John Lovett Doust—a daughter.
MACLEOD.—On Sept. 21, at Clevedon, Somerset, the wife of Dr. Alastair MacLeod—a daughter.
NAIRAC.—On Aug. 31, in Mauritius, the wife of Dr. M. L. Nairac—a son.
PIERCE.—On Sept. 21, in London, the wife of Dr. John Pierce—a daughter.
ROLLASON.—On Sept. 27, at Scunthorpe, the wife of Dr. W. N. Rollason—a son.
SCOTT.—On Sept. 18, in London, the wife of Dr. I. M. Scott—a son.
THOMS.—On Sept. 22, at Bognor Regis, the wife of Surgeon Commander Geoffrey Thoms, R.N.—a son.
VENNING.—On Sept. 25, in London, to Dr. Ruth Venning (née Barker), wife of Dr. G. R. Venning—a son and a daughter.

MARRIAGES

LEES—FAWCUS.—On Sept. 18, at Aston Clinton, Bucks, Norman Lees, M.B., to Pamela Joan Fawcus.
WETHERELL—MANN.—On Sept. 18, at East Budleigh, Geoffrey Wetherell, M.B., to Rosemary Mann.

DEATHS

BOULTON.—On Sept. 19, Norman John Boulton, M.R.C.S., aged 45.
FISHER.—On Sept. 25, at Barnton, Midlothian, Edward Fow Fisher, M.B. Lond., F.R.C.S., M.R.C.P.E., D.P.H.
GAVRONSKY.—On Sept. 24, Jacob Osip Gavronsky, M.D. Halle, aged 70.
GHOSH.—On Sept. 24, at Salford Royal Hospital, Jotindranath Ghosh, F.R.C.S.I., D.P.H., aged 61.
GIBSON.—On Sept. 16, Harold Edward Gibson, M.A., D.M. Oxfd.
POTTS.—On Sept. 25, at Woking, Surrey, Edmund Thurlow Potts, C.M.G., D.S.O., M.D. Edin., lieut.-colonel, R.A.M.C. retd.
SHUBIK.—On Sept. 20, 1948, at Oxford, Nancy Gwendolyn Shubik, M.R.C.S., D.P.H.

Digitized by Google

Notes and News

PHYSIOTHERAPY CONGRESS

THE congress of the Chartered Society of Physiotherapy, held in London from Sept. 22 to 26, was attended by official delegates from fifteen different countries, and a session was devoted to a discussion of international collaboration in physiotherapy.

The congress opened with a reception at the Apothecaries' Hall, and next day the inaugural address was given by Sir WILLIAM DOUGLAS, secretary to the Ministry of Health. Instead of asking "What is the National Health Service?" Sir William suggested, it was sometimes well to ask "When there is no National Health Service, what is there?" In early times when there was no organised medical aid life must have been painful and short. Even now in a progressive country like America about three-quarters of the population were without any kind of insurance against risks to health. That was the background against which we should consider our Act. After briefly surveying its provisions he turned to the question of where the physiotherapist comes in. The Ministry, he said, was fully alive to the importance of physiotherapy, particularly as part of rehabilitation, when the physiotherapist, as one of a team, was associated with the surgeon, the remedial gymnast, and the occupational therapist. There was a shortage of physiotherapists, and the Ministry and the society were doing all they could to help forward the creation of schools for the training of more. It was therefore all the more important that the physiotherapist's work should be used to the best possible advantage under conditions of control. Those who most needed help should have priority. Later there would be opportunities for domiciliary practice among those who could not come to hospital, but the Ministry felt that at first the physiotherapist's main work should lie in the hospitals and in the health centres.

We were faced, said Sir William, with an ageing population and limited man-power, and one of the fundamental facts emerging from a national survey of the health resources of the country was that we must make the best use of what we had. This thread ran through the whole service. Thus we must be careful that the hospitals able to deal with acute cases dealt with such cases and were not cluttered up by people for whom less highly skilled treatment would be suitable. It was possible to see how by a comprehensive grouping of health as a whole the Ministry or Government could plan on a national and wide basis.

At a luncheon held towards the end of the congress, with Lord HORDER in the chair, Mr. WALTER R. OWEN, chairman of the London Council, returned to the physiotherapist's rôle in our health services. He recalled that Lambeth—an L.C.C. hospital—was one of the first to employ "rubbers and spankers," as masseurs were irreverently called in those days. He knew what physiotherapists had contributed to our health in the past and he was sure that in the new National Health Service they would maintain their high professional standards. Dr. W. S. C. COPEMAN, chairman of the council of the society, said that though Mr. Owen had painted a brilliant miniature of the past he had left a blank canvas for the future which was daunting even to an amateur artist. Dr. Copeman agreed with Sir William Douglas that there were not enough members of the society to grapple with the work that lay before them and he recognised that some temporary dilution was therefore inevitable. But the society was anxious that permanent standards should not be permanently lowered, and to meet the situation it had offered to open a supplementary register. He believed that the Ministry's reply to this proposal might be expected in the not too distant future.

HOSPITAL GUIDE FOR LIVERPOOL REGION

ONE of the immediate tasks before the administrators of the National Health Service is to translate the Act and the statutory instruments of Whitehall into information about how Dr. Brown can arrange for Mr. Smith to be admitted to hospital and for Mrs. Jones to have a pair of spectacles. In their "preliminary information concerning hospital and specialist services" Liverpool Regional Hospital Board have successfully and succinctly changed national terms into local idiom. The booklet begins by setting out the members, committees, and senior officers of the board, and the members and addresses of secretaries of the hospital management committees. The hospitals administered by the board are listed in their groups and are also shown on a map of the area. Another section describes how services such as pay-beds, mass radiography, surgical appliances, and pathological facilities may be obtained. The second edition of the booklet was issued by the board in August from their temporary address at Alder Hey Hospital, Eaton Road, Liverpool, 11. A complete set of regional guide-books would be a valuable pendant to the Act.

INDEX FOR FILM RECORDS

PHOTOMICROGRAPHY on 35 mm. film is now a recognised method of copying documents, journals, and pictures either for space-saving storage or for convenient transport. A live filing system is needed if microfilm and filmstrip are to be used not only for dead documents and set lectures but also for the day-to-day purposes of hospitals, libraries, and photographic and scientific departments. The filing system devised by Filmdex Ltd., of 1, Wilton Mews, London, S.W.1, provides envelopes with pockets taking short strips of 35 mm. film, indexing sheets, and a binder to contain the envelopes and index. It seems to be convenient and is not expensive.

ASEPTIC DISPENSARY

THE increasing demand for sterile intravenous or intramuscular injections, and particularly for freshly compounded penicillin solutions or applications, is necessitating courses in aseptic techniques for pharmacists and special apparatus in their pharmacies. Any pharmacist of course may dispense the sterile preparations sent out in sealed containers by the manufacturers, but there will always be prescriptions which call for non-standard dosages, concentrations, or ingredients, and the pharmacist who dispenses penicillin for injection must first satisfy the requirements of the Therapeutic Substances Act with regard to asepsis. As an example of what is being done, Messrs. Boots have opened an aseptic dispensary above their branch on the north side of Piccadilly Circus. Here a specially trained staff work under surgically clean conditions in a room supplied with filtered air. The actual compounding is done in a glass "frame" covered with sterilised 'Nylon'; only the dispenser's gloved hands enter the frame, and he must see what he is doing through a small window at the top. About half of the 30 or so prescriptions dealt with daily contain penicillin.

SMOKE ABATEMENT

THE National Smoke Abatement Society has been holding its annual conference at Cheltenham this week. Sir George Elliston, who is succeeded as president by Lord Simon of Wythenshawe, said that his $2\frac{1}{2}$ years of office had seen some 25 million tons of coal "mined at great cost, transported at more cost—and then thrown away." But it had also seen some of the most important advances yet made towards ending the smoke evil, and certainly the most satisfactory growth of the society's own position and standing. Mr. Leslie Hardern remarked that "education and persuasion of the public today on any issue can be achieved more rapidly than ever before in history." But the task of achieving it has become much more complicated and extensive than ever before. To make effective use of all possible propaganda channels would cost the society £500,000 a year instead of the £1000 it was able to spend last year. An income of £20,000, however, would enable it to make use of the more promising methods.

The society's address is Chandos House, Buckingham Gate, London, S.W.1.

MEDICAL CARE IN RURAL AMERICA

DURING the last twenty years much attention has been paid in the United States to the problem of providing the American people with adequate medical care. Elaborate inquiries, notably those of the Committee on the Costs of Medical Care in 1928–31 and the National Health Survey in 1935–36, have revealed a "cultural lag" between the advances of medical science and the progress made in bringing the benefits of those advances to the general public. The results of the lag are most apparent among the rural population, which at the 1940 census numbered 57 million, forming 43·5% of the total population. This is made clear in a new book by Dr. Frederick D. Mott and Dr. Milton I. Roemer,[1] who show that though the American country worker and his

1. Rural Health and Medical Care. London: McGraw-Hill Publishing Co. 1948. Pp. 608. 39s.

Digitized by Google

family enjoy important advantages over the town-dweller (e.g., pure air, an abundant diet, outdoor exercise, and more temperate habits) these are counteracted by the prevalence of insanitary conditions and a lack of medical services. At the 1940 census, the professional personnel engaged in the prevention or cure of disease (doctors, dentists, nurses, midwives, pharmacists, and osteopaths) numbered 762,000, of whom only 18·6% lived in rural communities.

A masterly study of the conditions acting unfavourably on the health of rural Americans is followed by proposals for amendment. On the public-health side, the authors accept the proposal of the American Public Health Association that the nation should be organised into units of local health service with populations of not less than 50,000, receiving Federal grants depending upon efficient administration. On the clinical side, they recommend a wide extension of health insurance and of group medical practice. They realise that in order to make adequate medical care generally available it would be necessary to provide trained personnel and hospitals on a scale far more extensive than the present one, and that much would have to be done in the fields of technical training and hospital construction. They are, however, fertile in suggestions to meet the various difficulties that lie ahead, and their book, well arranged, well written, and remarkably interesting, is a valuable contribution to social medicine.

University of London

Dr. J. V. Dacie has been appointed to the readership in hæmatology at the Postgraduate Medical School of London as from Oct. 1, 1948.

Dr. Dacie took the M.B. Lond. from King's College Hospital in 1935, and the M.R.C.P. the following year. He has held a Medical Research Council research studentship and a Will Edmonds clinical research fellowship and he has also acted as resident pathologist at King's. During the war he was for a time a pathologist in the E.M.S. and later he served in the R.A.M.C. with the rank of major. Since 1946 he has been senior lecturer in hæmatology at the Postgraduate School. His published work includes papers on familial hæmostatic anæmia, nocturnal hæmoglobinuria, and blood-loss in battle casualties.

Mr. C. L. Foster, PH.D., has been appointed to the readership in biology at St. Mary's Hospital medical school as from Oct. 1. Since 1947 he has been senior lecturer in histology in the department of anatomy at the school.

University of Leeds

At recent examinations the following were successful:

M.D.—E. Cope (with distinction), Dorothy D. Jones, J. H. Kahn, S. Lask, H. Lee, S. Madden, R. H. Seville.

Final Examination for M.B., Ch.B.—H. Black, Ellen M. Chippindale, J. W. Daggett, M. Dales, R. England, Kathleen Gillen, Roxie Glossop, Edwina E. Green, D. C. Hall, R. T. Heylings, E. Menchovsky, C. H. Morris, Sarah L. S. Phillips, Marjorie Pitman, Elizabeth Pryce-Jones, P. J. Reynolds, P. D. Roberts, Etienne Sandford, C. J. Sharp, Barbara Welburn, A. B. Wharton, J. C. Woodrow, D. P. Wright.

Society of Chemical Industry

A joint meeting of the nutrition and microbiological panels of the society will be held on Wednesday, Oct. 13 at 6.15 P.M., at Gas Industry House, 1, Grosvenor Place, London, S.W.1, when Mr. E. F. Gale, PH.D., will read a paper on the Rôle of Vitamins and Metals as Co-enzymes in Bacterial Metabolism.

British Orthopædic Association

The annual meeting of the association will be held in Belfast from Oct. 21 to 23. The programme includes a discussion on the Painful Shoulder, to be introduced by Prof. George Perkins. Mr. S. A. S. Malkin will give his presidential address.

Demonstration of Contraceptive Technique

Mrs. Marie C. Stopes, D.SC., and Dr. Beddow Bayly will give a demonstration at the Mothers' Clinic, 108, Whitfield Street, London, W.1, at 2.30 P.M. on Thursday, Oct. 7. Doctors who wish to attend should apply for tickets in advance.

Royal Institute of Public Health and Hygiene

The series of lectures to be given at the institute, 28, Portland Place, London, W.1, this autumn beginning on Oct. 13 will include the following: Dr. W. G. Wyllie (Weaning and Mixed Feeding of the Infant), Dr. Peter Henderson (Epilepsy in Children), Dr. Fraser Brockington (Problem Families), Dr. N. L. Lloyd (Placing the Impaired Worker in Industry), and Dr. P. G. H. Gell (Food and Resistance to Disease). The lectures will be given on Wednesdays at 3.30 P.M.

Institute of Neurology

Dr. Gordon Holmes, F.R.S., is giving the inaugural address to the institute at the National Hospital, Queen Square, London, W.C.1, on Monday, Oct. 4, at 5 P.M. He is to speak on Incoördination of Movement.

West London Hospital

On Wednesday, Oct. 13, at 11.45 A.M. in the rheumatism department, Dr. Philip Hench (Mayo Clinic) will give a lecture on Psychogenic Rheumatism. Dr. Spencer Paterson, psychiatrist to the hospital, will also speak.

Association of Optical Practitioners

Mr. H. C. Weston, F.I.E.S., a member of the Industrial Health Research Board, will deliver the Ettles lecture to this association at the London School of Hygiene, Keppel Street, W.C.1, on Wednesday, Oct. 13, at 7.45 P.M. He is to speak on the Facilitation of Visual Tasks with special reference to Near Visual Problems.

Société Internationale de Chirurgie Orthopédique et de Traumatologie

At the fourth congress of the society, held in Amsterdam last month, Sir Harry Platt was elected president, and Dr. San Ricart (Barcelona) and Prof. E. Sorrel (Paris) vice-presidents. The next congress will be held in May, 1951, at Stockholm, with Prof. Richard Scherb (Zurich) as president of the congress.

Exhibition of Medical Photography

There will be an informal display of medical photographic apparatus and records at the department of medical photography of the Westminster Hospital medical school, 17, Horseferry Road, S.W.1, from Oct. 5 to 9 inclusive, from 10 A.M. to 4 P.M. Series of photographs will be used to show complete case-history recording, and recording of dermatological conditions.

Churches' Council of Healing

Beginning on Oct. 14, six lectures on the Christian Factor in Healing will be given at 7 P.M. on the second Thursday of each month at Friends House, Euston Road, London, N.W.1. The lecturers will include Dr. Cuthbert Dukes, Dr. Bodley Scott, Dr. R. Kenneth McAll, and Dr. Isabel Gough. Further particulars may be had from Mrs. Michael Thomas, Hughenden Manor, High Wycombe, Bucks.

Dr. Russell Reynolds has been elected an honorary fellow of the American College of Radiology.

Surgeon Captain W. J. Colborne has been appointed an honorary surgeon to the King in place of Surgeon Rear-Admiral J. A. O'Flynn who has retired.

Dr. Geoffrey Vevers, superintendent of the London and Whipsnade zoos, is to retire at the end of this year for reasons of health. Dr. Vevers joined the staff of the Zoological Society in 1919 as honorary parasitologist, and he was appointed to his present post in 1923.

CORRIGENDUM.—*Absorption and Excretion Studies with Radioactive Penicillin.* In the figure on p. 494 the penicillin was given by intramuscular injection, as stated in the text.

Appointments

BAIRD, I. M., M.B. St. And.: clinical assistant, medical unit, Sheffield Royal Hospital.

MACDONALD, D. G. C., M.B. Lond., D.M.R.: radiologist, Public Hospital, Tumaru, New Zealand.

THOMSON, C. S., M.B. Belf., D.P.H.: senior asst. M.O., public-health department, Norwich.

Lancashire County Council:

Asst. divisional M.O.:

ATKINSON, CONSTANCE, M.B. Manc., D.P.H.
BENNETT, HELEN, M.B. Manc., D.P.H.
CRAWSHAW, D. G., M.B. Manc., D.C.H., D.P.H.
DAVIES, J. B. M., M.B. Lond., D.P.H.
DOBSON, J. N., M.B. Edin., D.P.H.
GILLET, J. A., M.B. Lpool, D.P.H.
HAY, G. G. W., M.B. Aberd.
HIGGINS, GEOFFREY, M.B., B.SC. Leeds, D.P.H.
MCLEOD, W. J., M.D. Belf., D.P.H.
MILLAR, JANE, M.D. Glasg., D.OBST. R.C.O.G., D.P.H.
PATERSON, WILLIAM, M.B., D.P.H.
SHARPE, WILLIAM, M.B., B.SC. Glasg., D.P.H.
TOWNEND, MARY, M.B. Leeds, D.P.H.
WOOD, J. H., M.B. Aberd., D.P.H.

Digitized by Google

OCT. 9, 1948 PAGES 555 TO 594

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6528 LONDON: SATURDAY, OCTOBER 9, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Infantile Gastro-enteritis Treated with Streptomycin by Mouth
URSULA JAMES, M.R.C.P.
I. R. H. KRAMER, L.D.S.
with a statistical analysis of results by
P. ARMITAGE, B.A. 555

Survival Period of Patients with Cerebral Hæmorrhage Dying in Hospital
W. McI. ROSE, M.R.C.P. 561

Determination of Hæmoglobin: v. Precision of Colorimetric Methods
Prof. E. J. KING, D.SC., and others 563

Unexplained Thrombosis of the Internal Carotid Artery
H. R. I. WOLFE, F.R.C.S. 567

Intestinal Obstruction from Fibrous Stricture
P. KONSTAM, F.R.C.S.E. 569

PRELIMINARY COMMUNICATION

Tetraethylammonium Bromide in Renal Cortical Ischæmia
F. E. STOCK, F.R.C.S. 570

SPECIAL ARTICLES

Medical Education in the Ukraine
W. P. FORREST, L.R.C.P.E. 579

Medical Protection Society 582

REVIEWS OF BOOKS

Surgery of Abdominal Hernia. G. B. Mair, F.R.C.S.E. 571

Disorders of Sex and Reproduction. A. P. Pillay, M.B. 571

Advances in Enzymology and Related Subjects of Biochemistry. F. F. Nord 572

Emergencies in Medical Practice. C. A. Birch, F.R.C.P. 572

Endocrinology of Neoplastic Diseases. G. H. Twombly, M.D., G. T. Pack, M.D. 572

LEADING ARTICLES

UNDER TENSION 573

STREPTOMYCIN IN INFANTILE ENTERITIS 574

AMERICAN PLAN 574

ANNOTATIONS

A Hundred and Twenty-five ... 576
Process to Provide more Insulin. 575
Better Health and Stricter Ethics 576
Patients' Reading 577
Mechanical Artificial Respiration 577
For Smoother Running 578

LETTERS TO THE EDITOR

Christmas Gifts (Lord Webb-Johnson, P.R.C.S.) 585

Exsanguino-transfusion in Acute Leukæmia (Dr. A. Piney) 585

H. influenzæ Meningitis Treated with Streptomycin (Dr. K. Zinnemann) 585

Proprietary Medicines under the Act (Dr. A. Forster) 585

Charms (Lieut.-Col. P. V. Karamchandani, F.R.C.P.E.) 586

Letter to a Nephew 586

Private Patients not Admitted .. 586

Diagnosis and Treatment of Pancreatic Necrosis (Dr. S. E. Luczyński) 586

Compensation for Practices Depleted during War Service .. 587

How many Nurses? (Mr. John Cohen, PH.D.) 587

Diagnosis of Peptic Ulcer in General Practice (Dr. S. Lipetz) 587

Handling of Food (Dr. F. A. Belam) 588

Selected for Interview 588

Mumps with Severe Complications (Dr. H. D. Browne) 589

Subacute Bacterial Endocarditis (Dr. M. J. Meynell) 589

A Diploma in Venereology 589

Technique of Discussion (Dr. J. N. Glaister) 590

Immunisation against Whooping-cough (Dr. Donald Paterson) .. 590

DISABILITIES

14. Poliomyelitis 582

PUBLIC HEALTH

Plumbing in America 590

Food and Drugs (Milk and Dairies) Act 1944 591

Health in the Second Quarter 591

Notification of Infectious Diseases 591

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 584

OBITUARY

Alexander Wilson Gill 592

NOTES AND NEWS

University Stipends 592

A Scottish Hospital 592

Vitrellæ 592

The *B.P. 1948* Explained 592

University of Aberdeen 593

Royal College of Obstetricians and Gynæcologists 593

Lloyd Roberts Lecture 593

International Congress of Ophthalmology 593

Regional Hospital Boards 593

Nuffield Medical Fellowships 593

Medical Protection Society 593

Middlesex Hospital Medical School 593

Royal London Homœopathic Hospital 594

St. John's Hospital Dermatological Society 594

Royal Institute of Philosophy ... 594

British Association of Plastic Surgeons 594

Proper Use of the Health Service 594

King's College Hospital Medical School 594

Award for Gallantry 594

Diary of the Week 594

Appointments 594

Births, Marriages, and Deaths ... 592

Founded 1892 Assets exceed £120,000

The MEDICAL PROTECTION SOCIETY Limited

President: SIR ERNEST ROCK CARLING, F.R.C.P., F.R.C.S., F.F.R.

Established for the protection of the professional interests of medical and dental practitioners. Members receive advice and assistance in all matters affecting the practice of their profession and are afforded COMPLETE INDEMNITY against costs and damages in cases undertaken on their behalf.

Entrance Fee 10/-

Annual Subscription £1 Membership Exceeds 23,000

No entrance fee to those joining within 12 months of registration

An additional subscription will secure indemnity in respect of practice overseas

Full particulars and application form from—

The Secretary, VICTORY HOUSE, LEICESTER SQUARE, W.C.2. GERrard 4553 & 4814

Digitized by Google

EXCERPTA MEDICA

FIFTEEN JOURNALS CONTAINING PERTINENT AND RELIABLE ABSTRACTS IN ENGLISH OF ALL ARTICLES IN THE FIELDS OF CLINICAL AND EXPERIMENTAL MEDICINE FROM EVERY AVAILABLE MEDICAL JOURNAL IN THE WORLD

Section I	Anatomy, Anthropology, Embryology and Histology	*Section VIII*	Neurology and Psychiatry
Section II	Physiology, Biochemistry and Pharmacology	*Section IX*	Surgery
Section III	Endocrinology	*Section X*	Obstetrics and Gynæcology
Section IV	Medical Microbiology and Hygiene	*Section XI*	Oto-, Rhino-, Laryngology
Section V	General Pathology and Pathological Anatomy	*Section XII*	Ophthalmology
Section VI	Internal Medicine	*Section XIII*	Dermatology and Venereology
Section VII	Pediatrics	*Section XIV*	Radiology
		Section XV	Tuberculosis

The Lancet. '. . . The difficulties of collecting, every month, several thousands of abstracts, all needing careful editing, and many requiring translation into English, are not small, but the first two sections to issue their maiden numbers—*Dermatology and Venereology* and *Radiology*—show that a high standard has been set, and it seems likely that the *Excerpta Medica* will prove an important agent for disseminating knowledge of medicine.'

The British Journal of Radiology. '. . . The conception and execution of the scheme should command nothing but the highest admiration. . . . The serious student of both diagnostic and therapeutic radiology will find this publication essential for keeping abreast of the literature because, indeed, it is impossible to conceive of any other way of doing so.'

Write for a prospectus, or specimen copy of the section you require to

DEPT. T., E. & S. LIVINGSTONE, LTD., 16-17, TEVIOT PLACE, EDINBURGH, 1

Sole distributors for Great Britain and the British Dominions

DIETARY DEFICIENCIES

Although there seems to be no evidence of severe malnutrition in this country at the present time there are, in individual cases, manifestations such as lack of concentration, lassitude, chronic fatigue and nervous disorders, which appear to be caused by inadequate diets. Some of these symptoms may be signs of a deficiency of the B vitamins.

Marmite is a yeast extract containing naturally-occurring riboflavin (1.5 mg. per oz.) and niacin (16.5 mg. per oz.) as well as other factors of the B_2 group derived from yeast; these include pyridoxin, pantothenic acid, choline, biotin and folic acid.

The dietetic value of Marmite has long been recognised; it is prescribed extensively as a prophylactic measure in combating malnutrition.

MARMITE

yeast extract

Jars: 1-oz. 8d., 2-oz. 1/1, 4-oz. 2/-, 8-oz. 3/3, 16-oz. 5/9. Obtainable from Chemists and Grocers
Special terms for packs for hospitals, welfare centres and schools

Literature on application

THE MARMITE FOOD EXTRACT CO., LTD., 35 Seething Lane, LONDON, E.C.3

4842

Digitized by Google

INFANTILE GASTRO-ENTERITIS TREATED WITH STREPTOMYCIN BY MOUTH

URSULA JAMES
M.B. Lond., M.R.C.P.
ASSISTANT PHYSICIAN

IVOR R. H. KRAMER
L.D.S. R.C.S.
ASSISTANT PATHOLOGIST

PRINCESS LOUISE CHILDREN'S UNIT, ST. MARY'S HOSPITAL, LONDON

With a statistical analysis of results by

P. ARMITAGE
B.A.

Of the Medical Research Council Statistical Research Unit, London School of Hygiene and Tropical Medicine

IN an outbreak of gastro-enteritis investigated by us in the winter 1946–47 and reported to the British Pædiatric Association (James 1947) *Proteus vulgaris* was isolated from the stools in every case and believed to play a part in the ætiology. *P. morganii* and organisms of the salmonella and shigella groups were excluded.

In view of these findings and of reports from elsewhere that streptomycin given by mouth produces bacteriostasis throughout the gut, and that naturally occurring strains of *P. vulgaris* are usually sensitive to streptomycin, it seemed logical to give streptomycin by mouth in cases of gastro-enteritis associated with *P. vulgaris* in the stools which were not responding to routine treatment. It also seemed important to establish whether streptomycin given by mouth was of any value in cases where *P. vulgaris* was not found in the stools. Therefore such patients were given streptomycin by mouth when routine treatment was unsuccessful and the prognosis was grave. The ætiological factors in these cases were not known.

In April, 1947, as a preliminary investigation, streptomycin was given by mouth to two infants with mild diarrhœa associated with *P. vulgaris* in the stools. This was done solely to determine whether the organism could be eliminated from the stools by this method, but the enteritis was so mild that these cases are not included in the present series.

This report is based on thirty treated cases, which are considered in three categories :

Group A : cases from an outbreak of epidemic diarrhœa of the newborn.

Group B : cases from an outbreak of gastro-enteritis in a residential nursery.

Group C : cases of gastro-enteritis in this Children's Unit, including patients critically ill on admission and cases not responding to routine treatment.

Routine treatment of all cases, except those in group C critically ill on admission, consisted of an initial period of starvation for 24 hours, during which sterile water alone was given by mouth, followed by the gradual building up of milk feeds at the rate of 60 calories a day. When possible, expressed breast-milk was given ; otherwise half-cream or full-cream National Dried Milk was used according to the age of the child. All feeds were made up to 20 calories to the ounce, and extra water was given as needed. Sugar was not added to the feeds until the 3rd or 4th day. When intravenous fluids were indicated, one-fifth physiological saline with 5% glucose or a quarter physiological saline with 2·5% glucose was used ; and, if intravenous therapy was continued for longer than 24–48 hours, protein hydrolysate solution supplemented the glucose-saline solution. Vitamins by mouth were not given until full feeds had been reached.

Dosage of Streptomycin by Mouth.—To maintain a constant bacteriostatic concentration, the total daily dose of streptomycin was dissolved in sterile water, and an equal fraction was given immediately before each feed.

Cases 19 and 20 were given a total of 2 g. in 4 days. In view of the scarcity of streptomycin and the early disappearance of *P. vulgaris* from the stools it was hoped that a smaller dose would be adequate, and cases 12 and 13 received 1 g. in 4 days. However, the organism reappeared in 2 days ; therefore all other cases were treated with 2 g. in 7 days : 0·5 g. in the first 24 hours, and 0·25 g. in each subsequent 24 hours for a further 6 days. The higher initial dose was given because of the known tendency of organisms to become resistant to streptomycin in a short time.

It was found convenient to make up the streptomycin solution so that the fraction of the daily dose to be given before each feed was contained in 1 ml. The solution was given with a spoon or a pipette, or direct from the hub of a syringe, and appeared to be palatable. No vomiting could be attributed to the streptomycin.

We found that the children having streptomycin tolerated milk feeds well, and that these could be increased at the rate of 100 calories a day. When streptomycin was started during the later stages of routine treatment, no further period of starvation was necessary, and the feeds could be increased at the rate of 100 calories a day from the level already reached.

GROUP A : EPIDEMIC DIARRHŒA OF THE NEWBORN

An epidemic of diarrhœa broke out in a maternity hospital. Fig. 1 shows the progress of four treated cases compared with that of twenty-three control cases occurring in the same period and receiving routine treatment only. The four cases selected for streptomycin therapy were the most severe in the outbreak. Jaundice had developed in three of them on the 18th, 34th, and 7th days of life.

CASE 1 was a premature infant weighing at birth 3 lb. 3 oz. Diarrhœa started on the 20th day of life, the latest onset in this group. Stool cultures were negative, and after 19 days' routine treatment (two periods of starvation followed by increasing feeds with an interval of 7 days during which she had full feeds) there was a sudden deterioration in her condition, and she appeared moribund. Her response to streptomycin was dramatic, and she regained her greatest previous weight (a gain of 13 oz.) in 10 days.

CASES 2 and 3 were selected for streptomycin treatment because of the severity of the gastro-enteritis, the lack of response to routine treatment, and the development of jaundice.

CASE 4 did not become jaundiced, but the combination of dehydration with œdema and the lack of any response to routine treatment prompted the administration of streptomycin.

The average number of days taken to regain the greatest weight reached before the illness was 12 in the treated cases compared with 25 (minimum 12, maximum 43) in the twenty-three less severe cases (fig. 1).

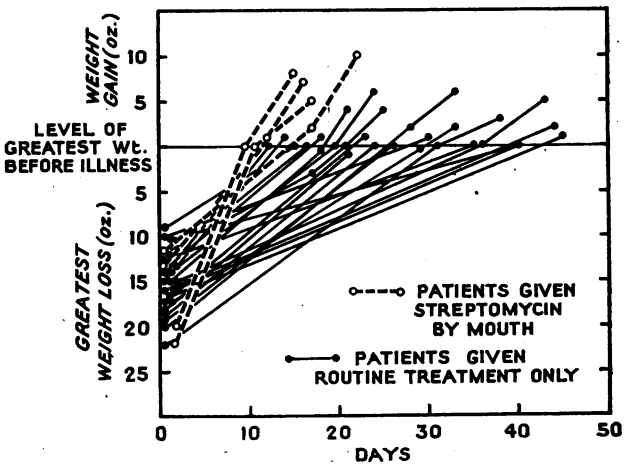


Fig. 1—Rates of return from points of greatest loss of weight to greatest weight reached before illness in epidemic diarrhœa of newborn (group A).

Digitized by Google

GROUP B: EPIDEMIC GASTRO-ENTERITIS IN A RESIDENTIAL NURSERY

An epidemic of gastro-enteritis broke out in a residential nursery among infants under 2 years of age, twelve children being affected.

The controls consisted of eight cases of moderate severity in infants aged from 2 weeks to 1¾ years. They were given routine treatment. The loss of weight was 3–23 oz. (average 12·6 oz.), and the recovery-rate (time taken to regain the greatest weight reached before the illness) was 6–60 (average 30·75) days (see the accompanying table and figs. 2 and 3). In five out of the eight cases *P. vulgaris* was isolated from the stools. All these children recovered, but their progress was slow.

The treated patients numbered four and were aged 3–11 months. Cases 5, 6, and 7 were much more severely ill than any of the controls. They each received routine treatment for 11, 5, and 4 days respectively, and at

RESULTS OF TREATMENT OF INFANTILE GASTRO-ENTERITIS WITH STREPTOMYCIN BY MOUTH

Group		Case no.	Sex	Age on admission	Birth weight before treatment (lb. oz.)	Max. weight before treatment (lb. oz.)	Max. weight loss (lb. oz.)	Length of history before admission (days)	Duration of routine treatment (days)	Clinical condition: Vomiting	Dehydration	Diarrhœa	Jaundice	Complications	Bacteriology of stool	Result: General progress	Result: Weight gain in 7 days (oz.)
Group A		1	F	3 wk.	3 3	4 15	12	—	19	Mod.	Mod.	Sev.	Mod.	None	Neg.	Excellent	7
		2	F	10 days	5 1	5 1	1 6	—	5	None	Sev.	Mod.	Mod.	None	Neg.	Excellent	17
		3	F	6 days	6 5	6 5	14	—	3	None	Mod.	Sev.	Mod.	None	*P. morganii*	Excellent	5
		4	M	12 days	7 7	7 7	1 4	—	4	None	None	Sev.	None	None	*P. vulgaris*	V. good	8
Group B		5	F	7 mos.	7 9	16 5	1 14	—	5	Mod.	Sev.	Sev.	None	None	*P. vulgaris*	V. good	14
		6	M	6 mos.	5 4	9 8	1 8	—	11	None	Slt.	Sev.	None	Prematurity and malnutrition	*P. vulgaris*	V. good	12
		7	M	3 mos.	8 0	10 8	1 2	—	4	Sev.	Sev.	Sev.	None	None	*P. vulgaris*	V. good	6
		8	M	11 mos.	7 2	15 0	14	—	4	None	None	Mild*	None	Inf. eczema, recurrent gastro-enteritis since 9 mos. old	*P. vulgaris*	V. good	36
Group C	Critically ill	9	M	4 mos.	10 10	11 13	2 13	24	—	Sev.	Sev.	Sev.	None	Right middle-lobe pneumonia	*P. vulgaris*	Excellent	14
		10	M	5 wk.	7 8	8 15	1 6	2	—	Sev.	Sev.	Sev.	None	None	*P. vulgaris*	Excellent	17
		11	F	8 mos.	7 12	?	2 9	5	—	Sev.	Sev.	Sev.	None	Pertussis→ pneumonia 2 wk. before gastro-enteritis	Neg.	Excellent	17
	Not responding to routine treatment	12	F	6 wk.	4 4	5 12	4	2	4	Slt.	None	Sev.	None	None	*P. vulgaris*	Good	10
		13	F	6 wk.	2 5	4 4	9	2	3	None	Mod.	Mod.	None	Anæmia	*P. vulgaris*	Slow	7
		14	M	2 mos.	8 4	8 15	1 0	—	4	Slt.	Slt.	Mod.	None	2 attacks of gastro-enteritis	*P. vulgaris*	V. good	19
		15	F	5 wk.	7 4	9 4	2 10	4	32	Sev.	Sev.	Sev.	Sev.	Bilateral mastoiditis	Neg.	V. good	15
		16	F	9 days	4 4	4 4	?	—	5	Mod.	Mod.	Sev.	Sev.	Died	Neg.	—	—
		17	F	3 mos.	9 0	10 6	5	70*	15	Mod.	None	Mod.	None	Recurrent gastro-enteritis	*P. vulgaris*	Good	17
		18	M	4 mos.	6 0	13 15	2 3	10	12	Sev.	Mod.	Sev.	None	Bilateral mastoiditis	*P. vulgaris*	None attributable to streptomycin	—
		19	M	4 mos.	6 10	12 8	1 4	—	8	Sev.	Sev.	Sev.	None	Intussusception and pyelitis	*P. vulgaris*	V. good	14
		20	M	4 mos.	6 12	11 2	12	3	16	None	None	Mod.	None	None	*P. vulgaris*	V. good	24
		21	M	5 mos.	?	15 1	1 10	8	4	Mod.	Sev.	Sev.	None	None	*P. vulgaris*	Good	5
		22	M	3 mos.	?	13 8	1 10	—	9	Mod.	Sev.	Sev.	None	Otitis media	Neg.	V. good	16½
		23	F	3 mos.	7 9	?	—	—	4	Sev.	Mod.	Sev.	None	Pneumonia and pyelitis	Neg.	Good	19
		24	M	3 mos.	6 6	8 11	11	—	4	None	Slt.	Sev.	None	Marasmus since 2 wk. old	*P. vulgaris*	Good	11
		25	M	6 mos.	?	17 12	4 0	—	17	Mod.	Sev.	Sev.	Slt.	Eczema	*P. vulgaris*	V. good	16
		26	M	9 mos.	7 7	19 12	2 1	3	5	Sev.	Slt.	Sev.	None	None	*P. vulgaris*	V. good	27
		27	M	13 mos.	?	23 5	2 12	5	4	Sev.	Sev.	Sev.	None	None	Neg.	V. good	31
		28	M	7 mos.	?	16 6	2 3	—	9	Sev.	Sev.	Sev.	None	Pneumonia and chickenpox	Neg.	V. good	17
		29	M	6 mos.	7 1	17 10	2 10	5	8	Sev.	Mod.	Sev.	None	None	Neg.	Good	18
		30	M	7 mos.	6 0	18 6	2 0	—	11	None	Slt.	Sev.	None	Eczema	*P. vulgaris*	Slow	5

* Recurrent gastro-enteritis.

Digitized by Google

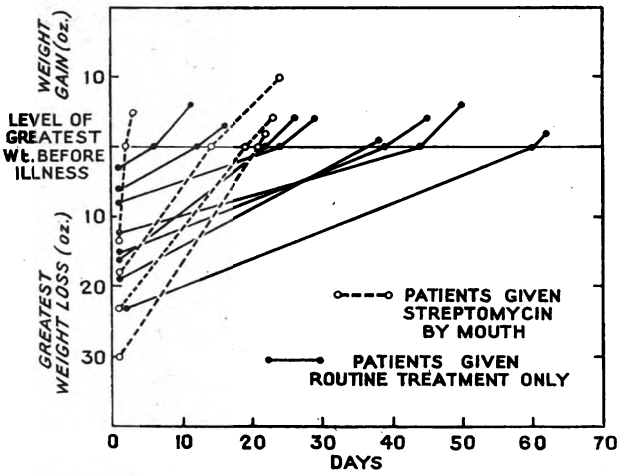


Fig. 2—Rates of return from points of greatest loss of weight to greatest weight reached before illness in an epidemic of gastro-enteritis in a residential nursery (group B).

the end of these times each child was deteriorating, the gastro-enteritis continuing, and the weight still falling. Streptomycin 2 g. in 7 days was then given by mouth in the way described, and all three cases responded well and quickly (fig. 4).

CASE 8, aged 11 months, had been in hospital with gastro-enteritis before admission to the nursery. On admission he was puny and lethargic and seemed mentally backward. He had minor recurrent attacks of passing loose offensive stools and lost 4–14 oz. with each bout. Even between attacks the stools tended to be pale and bulky, and *P. vulgaris* was isolated from them repeatedly. Streptomycin was given by mouth during one of these episodes, his weight gain was astonishing, and his stools became normal in 5 days and have remained so. He has had no further gastro-enteritis, and his general progress has been dramatic. He is now (10 weeks later) a normal child for his age (fig. 5).

The average recovery-rate in these four cases was 11·4 days—considerably shorter than that of the less severely ill controls:

	Controls	*Treated*
Average weight loss (oz.)	12·6	21·5
Average recovery-rate (days) ..	30·75	11·4
P. vulgaris present in stools ..	5	4
P. vulgaris absent from stools ..	2	0
Stools not examined	1	0
Average time for stools to become normal after streptomycin (days)	12·2	3·8
Age	2 wk. to 1¼ yr.	3 to 7 mos.

In this group it seems certain that streptomycin therapy speeded up recovery. Two patients were critically ill when it was started; one was not seriously ill but was not improving on routine treatment; and the fourth child had recurrent diarrhœa and was probably the source of infection in the nursery outbreak.

GROUP C: GASTRO-ENTERITIS IN THE CHILDREN'S UNIT

Patients Critically Ill on Admission

Cases 9, 10, and 11 were admitted in a critical condition with gastro-enteritis, and it was thought unwise to spend time in giving routine treatment alone.

CASE 9, a boy aged 4 months, was admitted from another hospital, where he had been treated for gastro-enteritis and had had 4 serious relapses in 24 days. On each occasion he had been starved and given intravenous and intraperitoneal fluids. Vomiting was copious, and his 5–8 stools a day were large, fluid, and offensive. His weight loss was over 2 lb. 3 oz. despite parenteral fluids (his greatest weight before illness was not known). Oral streptomycin was started, and feeds (100 calories in the first 24 hours with additional water) were given by mouth and retained, no further parenteral fluids being required. The stools improved and were normal in 4 days, the feeds being increased by 100 calories a day. The patient was fit for discharge 10 days after admission but had to remain in hospital another 10 days because of housing difficulties. During his 3 weeks' stay he gained 2 lb. and he gained a further 2 lb. in the 3 weeks following his discharge (fig. 6).

CASE 10, a boy aged 5 weeks, was admitted with severe gastro-enteritis of 2 days' standing. He had been offered full feeds but had taken only a few ounces in these 48 hours. His vomiting was copious, and the stools were large and entirely fluid (8 having been passed in the 10 hours before admission, and 12 in the 24 hours before that). On admission he was cold, collapsed, semiconscious, and grossly dehydrated. Intravenous fluids (2·5% glucose in *N*/4 saline) and streptomycin by mouth were given immediately. Water was given by mouth, and milk feeds were started 12 hours later, these being increased at the rate of 100 calories a day. Vomiting ceased after the first dose of streptomycin, and no further parenteral fluids were needed. No stools were passed for 48 hours. The patient's recovery was uneventful, and he was discharged 9 days after admission, having gained 25 oz. (fig. 6).

CASE 11, a girl aged 8 months, was transferred from a voluntary hospital, where routine treatment with intravenous fluids had been given for gastro-enteritis of 6 days' standing, this treatment being in accordance with our schedule. Her condition was considered hopeless; she had retained no fluids by mouth for 6 days, and was having copious fluid stools. She took streptomycin by mouth well and had no further vomiting, her stools improving in 3 days. Feeds were started on the 1st day, beginning at 100 calories and increasing to full feeds in 6 days. She was discharged 12 days after admission, having gained 20 oz., and a month later she had gained a further 4 lb. (fig. 6).

These were the only patients in the series to be given streptomycin on the day of admission. The speed of their response to streptomycin therapy was spectacular, and two of them needed no further parenteral fluids. They were ready for discharge in 9, 10, and 12 days.

Cases not Responding to Routine Treatment

The nineteen patients in this group were aged from 9 days to 13 months and were either admitted with gastro-enteritis or developed it in hospital. Five patients were under 3 months old and were all admitted with gastro-enteritis. Cases 12 and 13 were premature twins with birth weights of 4 lb. 4 oz. and 2 lb. 15 oz., and both developed gastro-enteritis within a few days of each other when 6 weeks old. Both responded well to streptomycin, not having improved on several days' routine treatment (fig. 7).

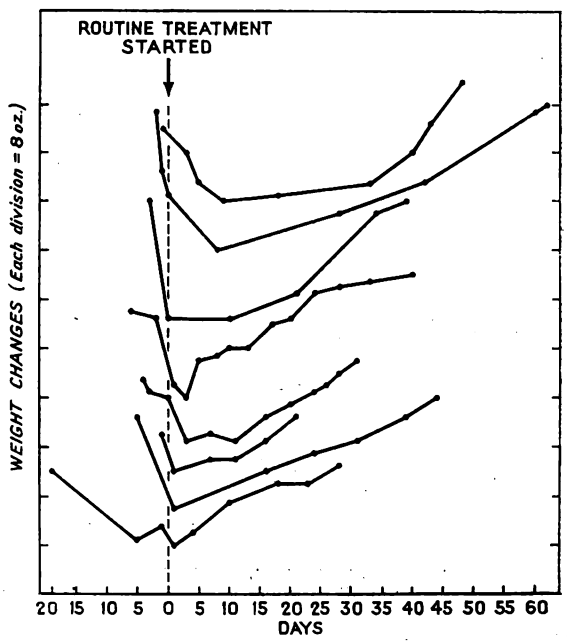


Fig. 3—Weight changes in 8 controls (group B).

Digitized by Google

CASE 14, a boy aged 2 months, had two recurrences of gastro-enteritis and did not respond to routine treatment during his third attack. The response to streptomycin was dramatic—he gained 19 oz. during the week, and his stools improved after 3 days, though they were still bulky and curdy 10 days later (fig. 7).

CASE 15, a girl aged 5 weeks, was one of the earliest cases treated. She had been admitted with a history of 4 days' diarrhœa and vomiting, and during the next 5 weeks she received rigorous treatment, including intravenous therapy, but she lost 2 lb. 2 oz. in weight. Her illness was complicated by bilateral mastoiditis (treated surgically) and pyelitis. She became deeply jaundiced, and her condition was critical. Her stool cultures were negative for *P. morganii* and *P. vulgaris* and for organisms of shigella and salmonella groups. All the patients previously treated had had *P. vulgaris* in their stools, but in view of the long period over which she had been treated and the gravity of her condition it was thought advisable to try streptomycin. Vomiting ceased from the 1st day, her stools improved, she needed no further parenteral fluids, and she gained 15 oz. during the week (fig. 8).

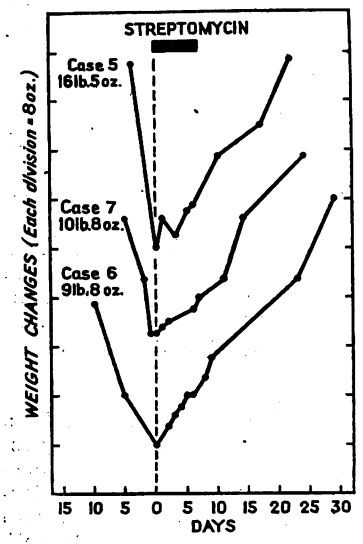


Fig. 4—Weight changes in 3 patients (group B) given streptomycin by mouth.

CASE 16, a girl aged 9 days, was admitted with 4 days' history of diarrhœa. Her stools had been frequent and fluid, and contained large amounts of bright blood. She was given routine treatment and injections of vitamin K with no improvement. Her total white-cell count at this time was 24,000 per c.mm. (eosinophils 24%). Streptomycin was then given by mouth and, though her diarrhœa and vomiting ceased and her general condition improved, she did not gain weight. She collapsed 7 days later, passed fluid stools containing large amounts of blood, and died in 24 hours (fig. 9). There had been no contact with other cases of diarrhœa, and her stool cultures were negative for all pathogenic organisms. Her father subsequently disclosed that he had had amœbic dysentery some time earlier but had not been in contact with the baby.

Necropsy (Dr. J. Bate) showed clear bloodstained fluid in the peritoneal cavity, the ileum intensely congested, and immediately proximal to the ileocæcal valve about 20 punched-out ulcers, most of them involving the mucosa only, but a few reaching the serous coat.

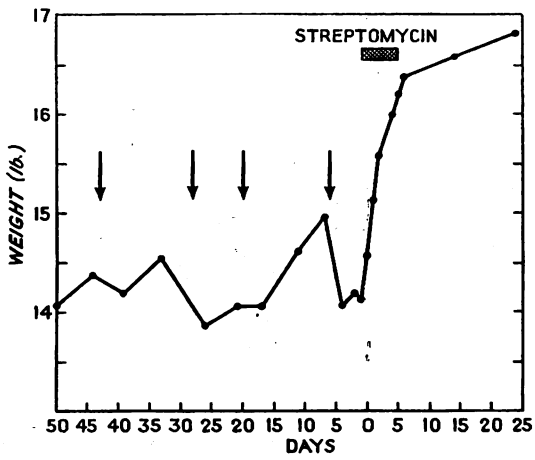


Fig. 5—Weight changes in case 8 (group B) given streptomycin by mouth: arrows indicate exacerbations.

This was the only case in the series with large amounts of blood in the stools, but it is interesting to note that Leisti (1947) found this in 11 (23·9%) of his 46 cases.

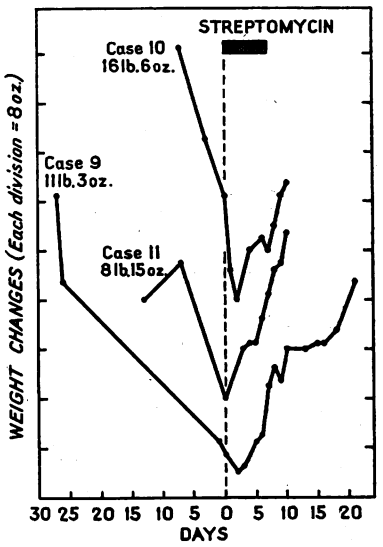


Fig. 6—Weight changes in 3 patients critically ill on admission (group C) given streptomycin by mouth.

There were eight patients aged 3–5 months. Case 18 did not respond to streptomycin, but the others responded well after a lack of response to routine treatment (fig. 10).

CASE 17 differed in that her gastro-enteritis was recurrent but not severe (cf. case 8 in group B). She was 2 weeks old when she had her first attack, and her stools had been pale, bulky, and offensive even between attacks. Her greatest weight before illness had been only 1 lb. 6 oz. above her birth weight. There was an exacerbation of her symptoms when she was 3 months old, and after 3 days' routine treatment streptomycin was given. She began to improve immediately, had no motion for 36 hours, then passed normal stools, and has continued to do so since. She was discharged 9 days later, having gained 18 oz. (fig. 10).

CASE 18 had had gastro-enteritis for a week, for which he had been admitted to another hospital. He had not improved and was transferred to us for treatment with streptomycin. Since his condition was not critical, we tried further routine treatment for another 6 days, without success, and he lost altogether 2 lb. 3 oz. Streptomycin was given by mouth, and next day a right otitis media appeared. Myringotomy was done and pus released. Five days later there was reddening and bulging of the left tympanic membrane, and myringotomy was done. During these 5 days he improved, the diarrhœa and vomiting lessened, and he gained 18 oz. In the subsequent 24 hours he lost 8 oz. and began to vomit again. Bilateral mastoidectomy was done, pus being found on both sides and *Bact. coli* obtained in pure culture from the right side. The patient's subsequent progress was satisfactory (fig. 11).

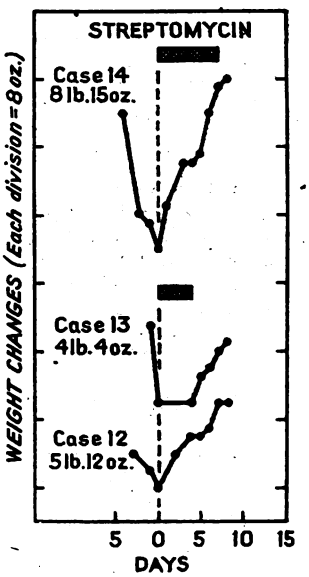


Fig. 7—Weight changes in 3 patients (group C) aged less than 3 months, not responding to routine treatment and given streptomycin by mouth.

In case 18 the recurrence of diarrhœa and vomiting was due to the parenteral infection, and this should have been recognised and treated before streptomycin was considered. In the presence of such an infection streptomycin by mouth is valueless.

There were six patients aged 6 months or more, none of whom had improved on routine treatment for a maximum of 17 days, a minimum of 4 days, and an average of 9 days (fig. 12). Five were admitted with gastro-enteritis, and one (case 25)

Digitized by Google

developed it in the ward, having been admitted with eczema.

CASE 25. After 5 days' routine treatment, during which diarrhœa and vomiting persisted, a bilateral mastoidectomy was done and necrotic bone was found on one side, but cultures from it remained sterile. The boy's symptoms continued, and despite intravenous and subcutaneous saline and intravenous protein hydrolysate, the weight loss over these 12 days was 4 lb. Streptomycin was given by mouth, and recovery was rapid and uneventful. In the week on streptomycin the patient gained 1 lb. 6 oz. (fig. 13).

The accompanying table shows the salient features of all the treated cases.

SUMMARY OF RESULTS

Twenty-eight of the thirty cases described responded satisfactorily to streptomycin given by mouth. One (case 16) died, and another (case 18) had bilateral mastoiditis, which was treated surgically, the child's recovery being in no way attributable to streptomycin.

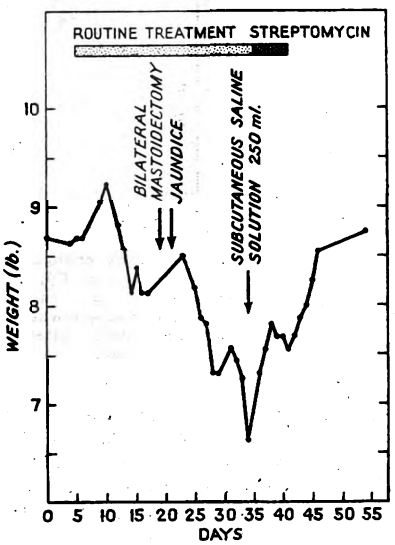


Fig. 8—Weight changes in case 15 (group C), not responding to routine treatment or to bilateral mastoidectomy and given streptomycin by mouth.

Weight seemed to be the most reliable measurable index of a child's progress. Since intravenous and subcutaneous saline was seldom necessary after starting streptomycin therapy, the gains shown in figs. 1–13 were not influenced by parenteral fluids, except in cases 5 and 10. In some cases the weight continued to fall during the first 24 hours of treatment with streptomycin, but thereafter the gains were spectacular. We considered the possibility of encountering these rapid gains in healthy children given streptomycin. Three such children, aged 4, 5, and 10 months, were weighed daily for 14 days, the same diets being given throughout, and streptomycin given by mouth in the same dosage as in our gastro-enteritis cases for the last 7 days. No difference was found in the rate of gain in the two weeks. The gains in weight of the treated patients and of the controls are compared below.

Stools.—In most cases improvement in the general condition preceded improvement in the stools. The consistence of the stools improved rapidly, but their frequency often persisted for 3 or 4 days, and they remained bulky and curdy for about 7 days. In cases where constipation developed after the administration of streptomycin no increase in toxæmia was observed, in contradistinction to that seen where diarrhœa is relieved with chalk and opium.

When streptomycin was given by mouth as described, there was a rapid fall in the number of organisms in the gut. In most cases a stage was reached, usually lasting for a few hours but occasionally for several days, when no growth could be obtained aerobically from the stools. If *P. vulgaris* was present it sometimes disappeared from the stools in as short a time as 4 hours. Preliminary investigation (by a method to be described elsewhere) showed that the streptomycin content of the stools could be as high as 1·5–2 mg. (1500–2000 units) per ml. Then the intestinal flora was gradually re-established, *Strep. fæcalis* often reappearing first and sometimes persisting in pure culture for several days.

It is important to bear in mind the possibility that organisms not usually present in the gut may become established there while the normal organisms are absent. One of us (I.R.H.K.) investigated the case of an infant given streptomycin by mouth who collapsed suddenly and died on the 3rd day of treatment. Cultures taken from the terminal ileum post mortem gave a pure growth of a streptomycin-resistant coagulase-positive *Staph. aureus*. The infant had a *Staph. aureus* conjunctivitis when streptomycin therapy was started.*

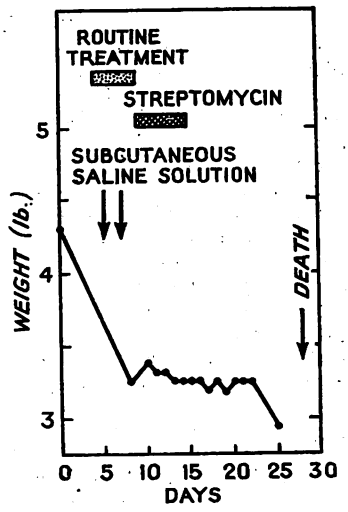


Fig. 9—Weight changes in case 16 (group C), not responding to routine treatment and given streptomycin by mouth. There were large amounts of blood in the stools.

Vomiting ceased in most cases after the first dose of streptomycin, and the appetite improved early in the course of treatment. This early cessation of vomiting is one of the greatest assets in the use of streptomycin in gastro-enteritis.

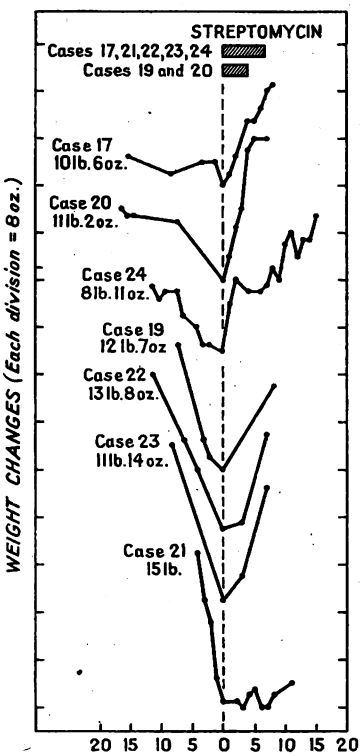


Fig. 10—Weight changes in 7 patients (group C) aged 3-5 months, not responding to routine treatment and given streptomycin by mouth.

Milk feeds were well tolerated when the child was having streptomycin, and it will have been noted that in the patients critically ill on admission to the Children's Unit, where streptomycin was given on the day of admission, feeds were given on that day at the level of 100 calories and increased by 100 calories a day. It is probable that, if cases were treated with streptomycin at the onset of gastro-enteritis, starvation could be safely omitted and generous feeds given throughout the illness.

Jaundice developed in five cases during routine treatment. It was most severe in case 15, when it lasted for 17 days, fading on the 4th day of the streptomycin course. All five patients recovered.

Stay in Hospital.—From the time that streptomycin was given, the patients' stay in hospital was very short. Most of them were fit to leave in 9–14 days, even in the most severe cases.

* This case is being described in detail in a later paper.—I. R. H. K.

Digitized by Google

COMMENT

Every effort must be made, when treating infants with gastro-enteritis, to exclude parenteral infection —e.g., mastoiditis. It should be remembered that, though for clinical purposes streptomycin is not absorbed from the gut, about 5% does enter the blood-stream, and this amount may be sufficient to render pathogens remote from the gut streptomycin-resistant, especially where there is a coincident urinary infection. We have demonstrated in one case a urinary level of streptomycin sufficient to render the infecting coliform organism grossly resistant. In such cases it might be wise to combine oral with intramuscular administration.

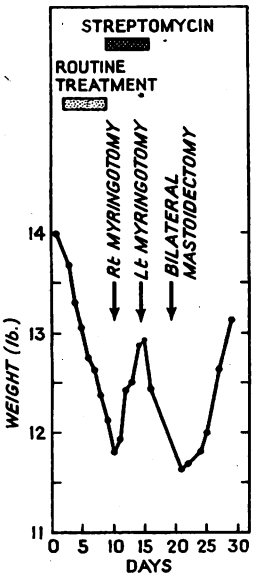


Fig. 11—Weight changes in case 18 (group C), not responding to routine treatment and given streptomycin by mouth. Bilateral mastoiditis was also present.

This investigation was started with the intention of treating gastro-enteritis associated with *P. vulgaris* in the stools, but it was found that cases with stools not containing this organism responded equally well. This experience agrees with that of Pulaski and Seeley (1948), who include among their non-tuberculous cases treated with streptomycin thirteen infants with epidemic diarrhœa of unknown ætiology. These infants were dehydrated and in shock, and they received 0·1 g. of streptomycin per lb. of body-weight daily, incorporated in their feeds, together with fluid and protein replacement. It was considered that streptomycin was the determining factor in saving at least four of the ten survivors.

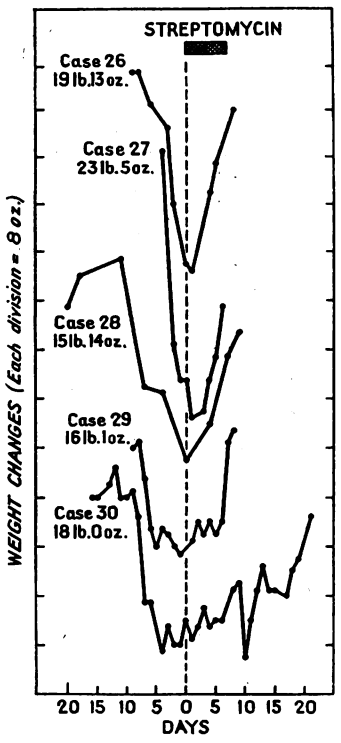


Fig. 12—Weight changes in 6 patients (group C) aged 6 months or more, not responding to routine treatment and given streptomycin by mouth.

Leisti (1947) gives an account of forty-six infants with gastro-enteritis whose stool cultures were negative; thirty-eight were full-term babies who developed gastro-enteritis when aged from 1 to 9½ months. A high proportion had blood in the stools (eight or 21%), in the vomits (seven or 18%), or in both (three or 8%), and of these eighteen cases twelve had been ill for less than 7 days. Streptomycin was given intramuscularly in doses of 10,000 or 20,000 units eight times a day, the total dosage varying from 120,000 to 8,300,000 units. Eight infants died, one did not respond to streptomycin but recovered, and two relapsed, one of whom responded to further streptomycin. The remaining eight infants were premature and developed gastro-enteritis when between 6 days and 8 weeks old. Six of these received intramuscular streptomycin 5000 units eight times a day (total dose, minimum 80,000 units, maximum 160,000 units), and two were given 5000 units of streptomycin by mouth eight times a day (total dosages 110,000 units and 140,000 units respectively). All responded but three relapsed including one who improved with further streptomycin. Leisti concluded that the use of streptomycin is advantageous in diarrhœa of infants, and that in severe cases it often leads to a rapid recovery and a steady weight gain.

Most likely, however, there are types of infective gastro-enteritis of infants which will not respond to streptomycin given by mouth, and among these will probably be those of virus origin.

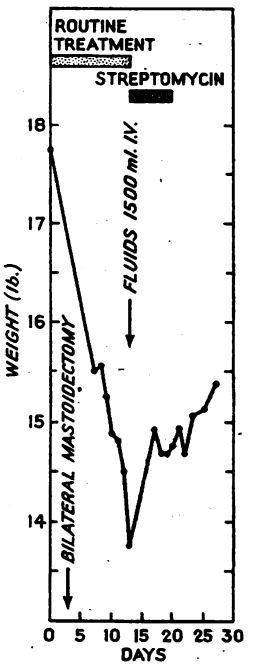


Fig. 13—Weight changes in case 25 (group C), not responding to routine treatment and given streptomycin after bilateral mastoidectomy.

GAINS IN WEIGHT OF STREPTOMYCIN-TREATED PATIENTS AND OF CONTROLS

(P. ARMITAGE)

In groups A and B, where it was possible to observe the progress of several other cases of gastro-enteritis in the same outbreaks as those from which the streptomycin-treated cases were drawn, the rates of weight gain from the lowest weight to the greatest weight reached before illness in streptomycin-treated cases and in controls have been compared.

The trials of streptomycin in these two outbreaks were not strictly controlled, since cases were not allotted at random or alternately to the treated and control groups. Since, however, the cases which were given streptomycin were chosen as being the more severe, we shall err in the right direction in testing whether there is a significant improvement in the rate of increase in weight in the treated groups. There was no significant difference between the mean maximum weights reached before illness in the treated and control groups in either outbreak.

In each of the two series the streptomycin-treated group showed not only a higher mean rate but also much greater variation about the mean than the controls. Since the usual statistical test for the difference between the means of two groups is of rather doubtful validity when there is a considerable difference between the variations within the groups, it was thought advisable to transform the criterion to the logarithm of the rate of increase in weight. This transformation tends to reduce this sort of discrepancy. For convenience in presentation, each logarithm was increased by unity, and this final variable has been denoted by x.

In group A (four streptomycin-treated cases and twenty-three controls) the following data were obtained:

Mean value of x for treated group = 1·152.
Mean value of x for controls = 0·773.
Mean square (or variance) for treated group = 0·04549.
Mean square (or variance) for controls = 0·03011.

The mean squares are obtained by summing the squares of deviations from the mean of each group, dividing by one less than the number of observations in the group

Digitized by Google

and taking the square root. They are measures of variation within each group. The two mean squares are not significantly different, and we may proceed with the standard test based on "Student's" t-distribution. The difference in means is 0·379, and its standard error is estimated as

$$\sqrt{\left\{\frac{3(0\ 04549)+22(0\cdot03011)}{25}\right\}\left(\frac{1}{4}+\frac{1}{23}\right)}=0\cdot0968.$$

$t=0\cdot379/0\cdot0968=3\cdot92$, on 25 degrees of freedom, a highly significant result. If the difference in means were due merely to sampling variation, and represented no real improvement, we should expect to find such a large value of t less than once in every 100 trials.

In group B (four streptomycin-treated cases and eight controls) the following values were found:

Mean value of x for treated group = 1·290.
Mean value of x for controls = 0·631.
Mean square for treated group = 0·12127.
Mean square for controls = 0·01747.

The two mean squares are significantly different in spite of the logarithmic transformation. The usual procedure of pooling the sums of the squares and calculating t is not justifiable in this case, but an estimate of the standard error of the difference in means may be taken as

$$\sqrt{\frac{0\cdot12127}{4}+\frac{0\cdot01747}{8}}=0\cdot1803.$$

The ratio of the difference to its estimated standard error is 0·659/0·180 = 3·65, a value sufficiently high to be regarded as significant. Such a high difference in means would arise by chance in less than 5 trials out of 100.

In view of the fact that the most serious cases were chosen for streptomycin treatment, we can safely say that the results indicate a real improvement in the treated groups.

SUMMARY

Streptomycin was given by mouth in thirty cases of infantile gastro-enteritis. Its effects were most striking in the critically ill cases, in cases of recurrent diarrhœa and vomiting, and in neonatal gastro-enteritis. Vomiting ceased early, weight was rapidly gained, the appetite returned, the stools improved, and there was almost immediate improvement in the general condition.

Streptomycin 2 g. by mouth in 7 days was given without producing toxic effects. It was palatable and well tolerated, even where there had been copious vomiting.

The administration of streptomycin by mouth does not obviate the necessity of treating parenteral infection, which may play a part in the causation of gastro-enteritis.

There is a danger that pathogens remote from the gut may be rendered streptomycin-resistant by the small amount of streptomycin that enters the blood-stream.

Streptomycin by mouth effectively eliminated *Proteus vulgaris* from the stools and was also effective in cases of gastro-enteritis where no pathogenic organisms were found.

Streptomycin by mouth shortened the course of gastro-enteritis to a considerable extent, the usual time of discharge from hospital being 9–14 days after the start of treatment, even in the very severe cases. This is a great asset in alleviating the pressure on beds and lessening the risk of cross-infection.

The early administration of streptomycin by mouth in gastro-enteritis may make it possible to omit a period of starvation and to give generous feeds throughout the illness.

It is not expected that all types of gastro-enteritis of unknown ætiology or those of virus origin will respond to streptomycin given by mouth.

We wish to thank the Medical Research Council's streptomycin trials committee for non-tuberculous diseases for the supplies of streptomycin; Sir Alexander Fleming and Dr. W. H. Hughes for their unfailing encouragement; the resident medical officers, nurses, and laboratory technicians who have contributed so much to this investigation; and Mr. P. Armitage for his statistical analysis.

REFERENCES

James, U. (1947) *Arch. Dis. Childh.* **22**, 180.
Leistl, P. (1947) *Ann. Med. intern. Fenn.* **36**, 575.
Pulaski, E. J., Secley, S. F. (1948) *J. Lab. clin. Med.* **33**, 1.

SURVIVAL PERIOD OF PATIENTS WITH CEREBRAL HÆMORRHAGE DYING IN HOSPITAL

W. McI. ROSE
M.D. Melb., M.R.C.P., M.R.A.C.P.
From the Department of Pathology and Bacteriology, University of Leeds

IN his classical paper on sudden death Spilsbury (1917) says that cerebral hæmorrhage is rarely a cause. This statement is generally accepted, for it accords with common clinical experience. But very little seems to have been written about the duration of life after cerebral hæmorrhage has occurred. Aring and Merritt (1935), in an article on the differentiation of hæmorrhage and thrombosis, pay scant attention to this point, and Newbill (1940) is content to state that hæmorrhage is more apt to be responsible when death takes place within twenty-four hours of the onset of symptoms.

My object here is to provide information about the duration of life after spontaneous cerebral hæmorrhage, including that from the rupture of an intracranial aneurysm. This is not of academic interest only, for early differentiation between hæmorrhage and thrombosis is necessary for effective use of systemic anticoagulants, as well as in assessing the results of treatment.

My facts are taken from the clinical and post-mortem records of the General Infirmary at Leeds in the eleven years 1936–46. During this time 7057 necropsies were performed, and in 227 (3·2%) of these some form of spontaneous cerebral hæmorrhage was found to be the main cause of death. In only 205 cases was there adequate information for the purposes of this paper, but apart from this no form of selection was used:

Site of hæmorrhage	*No. of cases*	*Cases suitable for analysis*
Cerebral hemispheres	103	92
Basal ganglia	47	43
Brain stem	36	32
Intracranial aneurysm	33	30
Cerebellum	8	8
	227	205

It has long been recognised that hæmorrhage may follow cerebral thrombosis after a period of a week or more, and in such cases it appears to result from an alteration in the nutrition of an arterial wall in relation to the area of softening. In this paper such hæmorrhages have been designated secondary, whereas for those in which no antecedent thrombosis appears to have been present the term primary is used.

FINDINGS

The details are set out in the accompanying table, but certain features require special comment.

Cerebral Hemispheres.—This site accounted for 45% of all cases, but no significant differences of survival time were found for different sites within the hemispheres. No patient with primary hæmorrhage who

Digitized by Google

ANALYSIS OF 205 CASES OF FATAL CEREBRAL HÆMORRHAGE IN PATIENTS WHO DIED IN HOSPITAL

Site of hæmorrhage	No. of cases	Sex		Age (years)		Survival		No. of cases in which heart weighed over 12 oz.		No. of cases with blood in cerebro-spinal fluid
		M.	F.	Range	Average	Range	Average	M.	F.	
Cerebral hemispheres:										
Primary	65	57	35	22–83	57	2–96 hr.	17 hr.	27	9	59
Secondary	27					7–16 days	12 days			24
Basal ganglia:										
Primary	40	25	18	31–81	58	3–90 hr.	21 hr.	12	5	34
Secondary	3					9–13 days	11 days			2
Brain stem	32	19	13	43–79	56	2–72 hr.	14 hr.	7	5	30
Aneurysm:										
Massive hæmorrhage	19	18	12	21–72	46	3–40 hr.	12 hr.	11	5	19
Repeated hæmorrhage	11					4–15 days	11 days			11
Cerebellum	8	5	3	52–76	61	8–96 hr.	46 hr.	2	0	6
Total	205	124	81	21–83	55	—	—	59	24	185

died in hospital survived longer than four days, and the total number of cases (65) is sufficient to make this finding probably significant. In the secondary group no death occurred before the seventh day after clinical thrombosis. Thus between primary and secondary cases there is as striking a difference in the time of death as there is in the underlying pathology.

Basal Ganglia.—In this site the main factor influencing prognosis is whether or not rupture into a ventricle takes place, a point that is made by Newbill (1940). In the 6 cases in which this did not happen the duration of survival averaged fifty-four hours, whereas the remainder are left with an average of fifteen hours.

Brain Stem.—Many examples of minor degrees of hæmorrhage in this site were noted in association with the larger and presumably earlier lesions seen in the hemispheres or the basal ganglia; but these are not included in this group. There are two examples of hæmorrhage into the brain stem without rupture into the subarachnoid space, and in these the duration of survival was sixty-two and fifty-four hours; if these are excluded, the average for the group falls to eleven hours, the least time of survival of all.

Intracranial Aneurysm.—This is the only form of cerebral hæmorrhage that has received much attention in the recent literature, and it is included in this paper because clinically, and occasionally at necropsy, it is impossible to differentiate it with certainty. Some aneurysms are indeed intracerebral in their site of rupture (Richardson and Hyland 1941), and in this series it is possible that some of the cases in younger subjects in which hæmorrhage into a hemisphere was found in the absence of cardiovascular disease may really belong to this group. There were 6 such patients under the age of 35, but in none of them is there any evidence of special search for an aneurysm having been made. The age range within the group is not quite so wide as in most published series, but Garland (1932) found a range of 11–80 years in a series of 32 cerebral aneurysms culled from the records of the same hospital at an earlier date; the average age of his patients is much the same as here—48 years as against 46 years. The difference in average age between this group and the cases of fatal hæmorrhage from other sites is not statistically significant.

In 16 of the 30 cases in this group the age was 45 or over, and it is a striking fact that in no less than 15 of these the heart weighed 12 oz. (340 g.) or more. Forbus (1930) has drawn attention to the importance of hypertension as the cause of the rupture in many of these cases of so-called developmental or "congenital" aneurysms of cerebral vessels, and the findings in the present series support his contention.

Cerebellum.—This is not a common site for hæmorrhage, and with one exception of eight hours all the patients lived more than twenty-four hours. The number of cases is too small for conclusions to be drawn.

Weight of Heart.—This has been noted at almost every necropsy; it is the only available evidence on which to assess the importance of hypertension as a causal factor, for in very few cases is the blood-pressure known before the cerebral catastrophe, and after it the value of any reading is open to doubt owing to the raised intracranial pressure which usually follows. It is generally accepted that the upper limit for the weight of the heart is about 11 oz. (312 g.), and this was used as the criterion of normal, though it is admitted that a variable, sometimes considerable, amount of fat is weighed with the heart at routine examinations. When the figures were examined on this basis, in 83 (40%) of 205 cases the heart weighed 12 oz. or more. Analysed according to sex there were 59 (48%) of 124 males and 24 (30%) of 81 females. The only hæmorrhage in which there was a striking association with increased heart weight was in the small group already mentioned, patients aged 45 or more who died from rupture of an intracranial aneurysm, of whom 15 out of 16 showed this association.

Blood in the cerebrospinal fluid is a sign which is sought for in the differentiation of cerebral hæmorrhage from thrombosis, yet in this series of 205 undoubted cases of cerebral hæmorrhage there were 20 (10%) in which no blood was found in the subarachnoid space at necropsy. In 3 cases rupture into a lateral ventricle had taken place, but the presence of clot in the iter or in the foramen of Munro had prevented the further escape of the blood. The other cases in this subgroup all tended towards the longer survival period as shown in the table, and clinically they had been regarded as thromboses.

DISCUSSION

Rather more than 80% of patients with cerebral hæmorrhage of primary type dying in hospital do so within twenty-four hours of the onset. Massive rupture of an aneurysm and hæmorrhage into the brain stem are associated with the shortest average duration of survival, whereas hæmorrhage into the cerebellum has the longest; in no instance did death take place in less than two hours in the 205 cases. This justifies the impression of clinicians and pathologists that cerebral hæmorrhage is rarely a cause of sudden death.

Digitized by Google

In so far as the weight of the heart post mortem is of value as an indication of hypertension during life, there is no striking association between heightened blood-pressure and cerebral hæmorrhage, save in the one small group mentioned above.

The fact that as many as 10% of fatal cases of cerebral hæmorrhage may not show free blood in the subarachnoid space does not appear to be generally appreciated.

Another point is the clear-cut difference between primary and secondary cerebral hæmorrhage as defined earlier; this would obviously be of some significance if any substantial series of cases of cerebral thrombosis were submitted to treatment with systemic anticoagulants.

SUMMARY

The clinical and necropsy records of 205 unselected cases of cerebral and cerebellar hæmorrhage, including intracranial aneurysm, in patients dying in hospital, were examined to determine the average duration of life after the onset of symptoms.

The shortest time before death took place was two hours, and over 80% of patients were dead within twenty-four hours.

Hæmorrhage into the brain stem and massive rupture of an intracranial aneurysm were associated with the shortest survival period, while hæmorrhage into the cerebellum had the longest.

There was no evidence that cardiac hypertrophy was especially frequent save in cases of subarachnoid hæmorrhage due to ruptured aneurysm in persons over 45 years of age.

REFERENCES

Aring, C. D., Merritt, H. H. (1935) *Arch. intern. Med.* **56**, 435.
Forbus, W. D. (1930) *Bull. Johns Hopk. Hosp.* **47**, 239.
Garland, H. G. (1932) *J. Path. Bact.* **35**, 333.
Newbill, H. P. (1940) *J. Amer. med. Ass.* **114**, 236.
Richardson, J. C., Hyland, H. H. (1941) *Medicine*, **20**, 1.
Spillsbury, B. H. (1917) *Practitioner*. **98**, 132.

DETERMINATION OF HÆMOGLOBIN

V. PRECISION OF COLORIMETRIC METHODS

E. J. KING M. GILCHRIST I. D. P. WOOTTON
Postgraduate Medical School of London

R. DONALDSON R. B. SISSON
National Physical Laboratory, Teddington

R. G. MACFARLANE H. M. JOPE J. R. P. O'BRIEN
Radcliffe Infirmary, Oxford

J. M. PETERSON D. H. STRANGEWAYS
University of Wales, Cardiff

THE reliability of different colorimetric methods of estimating hæmoglobin has been examined by Macfarlane et al. (1948). Most of these methods were in common clinical use. Included in this survey were early models of a "grey-wedge photometer" which showed considerable promise and has since been developed.* A preliminary account of its construction has already been published by King (1947), and it is hoped to provide more details in a later communication. In a similar investigation to be described here, the reliability of accurate instruments for measuring light absorption has been compared, the grey-wedge photometer being included. Several derivatives of hæmoglobin have been tested with the object of finding the most suitable for clinical and laboratory use.

Blood samples from 11 male and 10 female normal adults have been examined in these experiments. Hæmoglobin determinations by means of iron analyses, oxygen capacities, and carbon-monoxide capacities were carried out on all the bloods. With these values as a standard of reference, various hæmoglobin derivatives were tested in the most precise instruments available, and the results compared with those obtained with the grey-wedge photometer.

* It is expected that this instrument will soon be available commercially.

APPARATUS

VISUAL INSTRUMENTS

Duboscq Colorimeter used as Photometer.—The instrument used was a Leitz two-stage compensating colorimeter illuminated with a mercury-discharge lamp. A grey screen (density 1·0) was inserted on one side of the instrument and the solution on the other. The field was viewed through an Ilford mercury green (807) filter, and several readings were taken with the screen first on the left side and then on the right side of the instrument, the solution depth being adjusted until a match was obtained. In this way the instrument was used as a photometer as described by King et al. (1937). The illumination was almost monochromatic, and the viewing conditions were considered the best obtainable.

Autenrieth Wedge Colorimeter.—The models used were manufactured by Hellige, of Freiburg, and were used with those procedures for which a standard solution can be made. Hollow glass wedges were filled for each set of experiments with the standard solutions and sealed off. The test solution was contained in a 1 cm. glass cell.

Autenrieth Colorimeter as Photometer.—The Autenrieth colorimeter is readily adapted for use as a grey-wedge photometer by the substitution of a straight neutral grey wedge for the hollow glass wedge. Grey wedges of the appropriate size were made by Messrs. Ilford with an optical density range of 0–1·2 D. A light filter (Ilford mercury green or spectrum green) was placed in the eye-piece. The instrument was similar in design and operation to the annular grey-wedge photometer described below.

N.P.L. Colour Comparator.—The instrument, which was used to determine the strengths of the carboxyhæmoglobin solutions on the Haldane scale, is essentially the same as that described by Donaldson et al. (1943). Light from a single lamp is reflected by two white screens along two paths, in one of which is the specimen tube which can be interchanged with the B. S. Haldane standard tube; in the comparison path is a movable hollow wedge filled with carboxyhæmoglobin. The two beams are then viewed in a Lummer-Brodhun photometric field of about 15° angular subtense at the eye. Brightness variation in the comparison field is obtained by rotating one of the white screens. In operation the wedge is moved until there is a colour match first with the standard and then with the specimen which takes its place. From the wedge settings and gradient the concentration of the specimen is obtained as a percentage of the standard. Since some blood samples are slightly browner than the B.S. standard tubes, a movable pale-green wedge is provided on the comparison side to compensate for the abnormality and enable an accurate colour match to be made.

Grey-wedge Photometer.—Two beams of light pass through a diffusing screen and a monochromatic light filter; in this case an Ilford mercury green (807) filter was used. The beams then traverse symmetrical paths through the photometer to illuminate adjacent optical fields viewed with an eye-piece. One beam passes through, and is strongly absorbed by, the coloured solution contained in a 1 cm. glass cell; the other beam passes through a segment of the annular grey wedge. Both optical fields are therefore illuminated with green light, and a brightness match can be obtained by rotating the wedge and so altering the segment of the wedge in the beam. The "photometric end-point" or match may be approached from either side—i.e., from darker to lighter as well as from lighter to darker—and by rotating the grey wedge back and forth over the "end-point" an accurate match can be obtained. During matching the photometer is held squarely in front of a brightly illuminated window or a strong electric light. The circular grey wedge (0–1·2 D) is mounted in a metal holder whose circumference is marked in divisions.

PHOTO-ELECTRIC INSTRUMENTS

N.P.L. Spectrophotometer.—Spectral absorptions were determined on the spectrophotometer at the National Physical Laboratory. The main features of the instrument are as follows. (1) A double monochromator system: the second spectroscope serves as a stray light filter to improve the spectral purity of the emergent monochromatic light. (2) A potassium vacuum-emission photo-cell with valve amplifier is used as detector. The potential drop across a high grid leak is

Digitized by Google

TABLE I—NORMAL ADULT MALE BLOODS: COMPARISON OF GASOMETRIC METHODS WITH IRON ANALYSES

(All results are expressed as g. of Hb per 100 ml. of blood; conversion by means of Hüffner factors)

Blood no.	Iron analysis		Gas analysis				
	$TiCl_3$ titration		Van Slyke O_2			Van Slyke CO	Van Slyke CO after reduction
	P.M.S.L.	Oxford	P.M.S.L.	Cardiff	Oxford	Oxford	Oxford
1	15·31	15·24	14·86	..	..	15·12	15·30
2	16·39	16·38	15·88	..	16·00	16·28	16·43
3	15·66	15·89	15·33	..	15·32	15·49	15·98
4	15·63	15·51	15·01	15·00	14·98	15·31	15·75
5	15·36	15·19	14·95	15·08	14·88	15·03	15·49
6	16·15	16·22	15·50	15·74	15·57	15·78	16·28
7	17·25	17·19	16·69	16·71	16·82	16·97	17·20
8	16·72	16·57	16·25	16·41	16·48	16·42	16·64
9	15·48	15·28	15·20	15·08	14·94	15·14	15·29
10	14·98	14·59	14·56	14·40	14·55	14·55	14·81
11	17·12	16·65	16·56	16·49	16·33	16·79	17·09
Average	16·00	15·88	15·53	..	..	15·72	16·02

measured on a potentiometer to give the amount of light on the photo-cell. (3) Light from a battery-operated car headlamp is focused on the entrance slit. The output of the lamp remains constant to within 0·05%.

Photo-electric Colorimeters.—The King (1942) single photo-cell instrument was equipped with an optical glass cell of 1 cm. depth, a 4 mm. Chance OGR I glass light-filter, and a Tinsley 4500 H galvanometer. A Hilger Spekker absorptiometer was used with Ilford spectrum yellow-green light filters. These instruments were used at the Postgraduate Medical School of London.

OTHER APPARATUS

Spectrographic Instrument.—In one series of experiments spectral curves were obtained at Oxford with the Hilger medium quartz spectrograph.

Gasometric Apparatus.—The standard Van Slyke and Neill (1924) manometric apparatus was used at the Postgraduate Medical School of London, at Cardiff, and at Oxford, and, in addition, Warburg manometers were used at the Postgraduate Medical School of London.

Glassware.—Standard volumetric flasks of "A" quality were used. The calibrations were checked by weighing empty, and filled with distilled water. Ostwald-Folin pipettes, calibrated by weighing "to contain" were used for the measurement of all blood samples; errors in the delivery of such a viscous fluid were eliminated by rinsing the pipette into the receiver with distilled water. For other operations standardised delivery pipettes were used.

METHODS

All specimens were taken by one of us (R. G. M.) at the Radcliffe Infirmary, Oxford. A tourniquet was applied to the upper arm, a 16-gauge needle inserted into an antecubital vein, the tourniquet removed, and blood allowed to pass through a short rubber tube into a bottle containing mixed potassium and ammonium oxalates. The donors were healthy males and females aged 20–40; about 300 ml. was taken from each subject. After thorough mixing, and with precautions to avoid sampling errors, the blood was divided into three parts and placed in screw-cap bottles, whose caps, lined with 'Cellophane,' were tightly screwed on. Bottles were then dispatched by mail to London and Cardiff and were received by the first delivery next morning. Analyses in these laboratories were therefore begun about twenty-four hours after the blood had been taken; those at Oxford were completed on the day the blood was taken.

"Base-line" Methods.—At the Postgraduate Medical School of London, titanous-chloride titrations of the iron-containing residues after dry ashing were carried out according to the analytical procedure of Delory (1943) as modified by King et al. (1948). At Oxford Klumpp's (1934) method was used. The gasometric methods described by Peters and Van Slyke (1930) were followed in all samples. All these methods, together with the Warburg-manometer technique of oxygen capacity, have been fully discussed by King et al. (1948). In all cases the results of these "base-line" analytical methods were converted into hæmoglobin concentrations by means of Hüffner's (1894) factors—i.e., hæmoglobin contains 0·334% iron; 1 g. of hæmoglobin = 1·34 ml. of oxygen or of carbon monoxide.

Colorimetric Hæmoglobin Methods.—Oxyhæmoglobin, carboxyhæmoglobin, cyanmethæmoglobin, acid hæmatin, alkaline hæmatin, and cyanhæmatin were prepared exactly as described by King and Gilchrist (1947) and by Macfarlane et al. (1948).

Time of Reading Colours.—The oxyhæmoglobin, acid-hæmatin, and alkaline-hæmatin colours are preferably read at a definite time after their formation; they were therefore

TABLE II—NORMAL ADULT MALE BLOODS: COEFFICIENTS OF VARIATION FROM IRON ANALYSES

Methods	Place	No. of blood samples	No. of observers	—					
Gasometric:				O_2 capacity		CO capacity		CO capacity after reduction	
Van Slyke	P.M.S.L.	11	..	1·42		..		..	
	Cardiff	8	..	1·05		..		..	
	Oxford	10	..	1·00		0·63		1·32	
Colorimetric and photometric:				HbO_2	HbCO	Cyan-metHb	Acid hæmatin	Alkaline hæmatin	Cyan-hæmatin
Grey-wedge photometer	P.M.S.L.	8	6	0·61	0·62	1·09	0·76	1·56	0·51
	Cardiff	6	4	1·46	0·77	..	1·64	1·07	..
	Oxford	5	10	0·85	0·69	..	0·42	2·95	..
Duboscq colorimeter as photometer	P.M.S.L.	11	3	2·97	2·03	1·68	1·72	2·40	1·64
Autenrieth colorimeter	Oxford	5	10	..	0·91	..	1·35	..	..
	Cardiff	6	4	..	1·59	..	1·59	..	..
Autenrieth colorimeter as photometer	Oxford	5	10	..	1·10	..	0·72	3·46	..
	Cardiff	6	4	..	1·20	..	1·65	..	..
Spectrophotometer	N.P.L.	10	..	1·45	1·26	1·25	1·68	2·56	0·59
	Oxford	11	..	1·65	..	..	..	..	..
Colour comparator	N.P.L.	10	2	..	0·78	..	..	..	..
King photo-electric colorimeter	P.M.S.L.	11	..	1·89	1·47	1·39	1·56	0·43	0·66

Digitized by Google

TABLE IV—NORMAL ADULT FEMALE BLOODS: COEFFICIENTS OF VARIATION FROM IRON ANALYSES

Methods	Place	No. of blood samples	No. of observers	O_2 capacity		CO capacity		CO capacity after reduction	
Gasometric:									
Van Slyke	P.M.S.L.	10	..	1·05		1·86		1·46	
	Cardiff	10	..	1·23		..		..	
Colorimetric and photometric:				HbO_2	HbCO	Cyan-metHb	Acid hæmatin	Alkaline hæmatin	Cyan-hæmatin
Grey-wedge photometer	P.M.S.L.	10	6	1·62	1·18	1·16	3·46	1·98	1·24
	Cardiff	10	4	1·64	3·33	..	2·54	2·26	..
	Oxford	10	10	1·36	1·43	..	2·38	0·62	..
Duboscq colorimeter as photometer	P.M.S.L.	10	2	0·97	2·11	1·64	2·71	1·20	3·50
Spectrophotometer	N.P.L.	10	..	0·66	0·97	1·76	1·73	1·35	0·71
Colour comparator	N.P.L.	10	2	..	0·88	..	..	..	..
King photo-electric colorimeter	P.M.S.L.	10	..	0·70	0·98	1·60	1·66	1·61	1·00
Spekker absorptiometer	P.M.S.L.	10	..	1·05	2·15	2·95	3·19	1·91	3·29

read during the morning. The carboxyhæmoglobin, cyanhæmatin, and cyanmethæmoglobin colours were read later during the afternoon.

All visual instruments were read by several observers, the number varying from 2 to 10 (tables II and IV). To avoid the effects of fatigue as much as possible, the various instruments and colours (subject to the condition mentioned above) were taken in random order. As a routine, each observer read each colour in each instrument 5 times, and in the case of the Duboscq colorimeter each observer made 5 readings with the test solution on one side and 5 with it on the other. Thus 20–50 separate estimations were available for calculating the mean reading of any colour in any visual instrument.

RESULTS

"*Base-line*" *Results.*—The hæmoglobin concentrations of the various blood samples, derived from the results of the iron and gasometric analyses, are termed "base-lines." These figures are considered the most fundamental estimates available of the hæmoglobin concentrations and are used therefore as standards against which the precision of the instrumental results can be assessed. Tables I and III give the base-line results for the male and female blood series, each value being the mean of duplicate and sometimes triplicate analyses. In general the results calculated from oxygen and carbon-monoxide capacities are 2–3% lower than those derived from iron analysis, though preliminary reduction raises the carbon-monoxide capacity until it is almost equivalent to the latter. This discrepancy is discussed by King et al. (1948).

Instrumental Results.—One object of these experiments was to determine which of the colorimetric hæmoglobin methods would reflect most accurately the precision base-line analyses. The reliability of any colour, however, is affected by many instrumental factors, and it was therefore necessary to test each hæmoglobin derivative in the several instruments. The scatter of individual readings in various instruments has already been reported (Macfarlane et al. 1948), and information on this is not primarily sought. Of more interest was the "true reading" of the instrument, which in the case of photoelectric instruments is the actual reading obtained. For visual instruments the mean of the 20–50 readings obtained by the several observers was considered the "true reading."

The data obtained, then, consisted, for each derivative measured in any instrument, in a series of "true readings" corresponding in each case to the accurate hæmoglobin determinations by the base-line methods. The quotients obtained by dividing the "true reading" by the corresponding hæmoglobin concentration were, with an accurate instrument, substantially constant, and the degree of constancy furnished a measure of the reliability of the instrumental "true readings." At first each of the different base-line methods was used to obtain such a series of quotients, but it very soon became apparent that the quotients obtained by using the results of the iron analyses were significantly lower, and varied less, than those derived from the gasometric methods. For this reason it is thought that iron analysis furnishes a more accurate base-line method than does any other available method, and all results presented here are calculated from quotients which have as denominator the hæmoglobin concentration obtained by iron analysis.

Each series of quotients was reduced to standard form by calculating first its standard deviation and then the Pearson coefficient of variation, defined as the standard deviation (σ) expressed as a percentage of the mean (M)—i.e., $C.V. = 100\sigma/M$ (tables II and IV).

Quotients were similarly formed on the results of the gasometric base-line methods, and the coefficients of variation so obtained are also given. They enable a

TABLE III—NORMAL ADULT FEMALE BLOODS: COMPARISON OF GASOMETRIC METHODS WITH IRON ANALYSES

(All results are expressed as g. of Hb per 100 ml. of blood; conversion by means of Hüffner factors)

Blood no.	Iron analysis	Gas analysis			
	$TiCl_3$ titration	Van Slyke O_2		Van Slyke CO	Van Slyke CO after reduction
	P.M.S.L.	P.M.S.L.	Cardiff	P.M.S.L.	P.M.S.L.
1	16·04	15·42	15·50	15·19	15·85
2	13·98	13·45	13·85	13·18	13·82
3	12·93	12·47	12·71	12·74	13·04
4	13·49	12·89	12·99	12·94	12·95
5	12·43	12·17	12·29	12·27	12·26
6	12·94	12·77	12·84	12·65	12·73
7	12·29	12·04	12·22	12·11	12·25
8	11·81	11·53	11·77	11·60	11·70
9	13·80	13·34	13·63	13·36	13·49
10	13·63	13·20	13·27	13·13	13·18
Average	13·33	12·93	13·11	12·92	13·13

Digitized by Google

comparison to be made between the reliability of gasometric and colorimetric methods of estimating hæmoglobin.

Spectrophotometric Results.—For all the samples of blood (11 male and 10 female) the spectral absorptions of each of the six hæmoglobin derivatives were measured on the N.P.L. spectrophotometer. Values were determined at each 10 mμ throughout the visible spectrum.

The coefficients of variation (tables II and IV) are based on absorption measurements at 540 and 560 mμ; detailed information on the spectral data will be reported elsewhere.

DISCUSSION

This investigation has been based on the principle used in previous work on the reliability of methods for determining hæmoglobin (Macfarlane 1945, King et al. 1944, Macfarlane et al. 1948). This is the comparison of the results obtained by several observers using the less precise routine methods with the results obtained on the same blood sample by the most precise methods available. In the present investigation some of the instruments tested were more elaborate and precise than the average routine determination of hæmoglobin requires, but their comparison with simpler procedures is instructive. For this reason the performance of two spectrophotometers, two photo-electric colorimeters, and standard visual colorimeters and photometers has been investigated in comparison with that of the small neutral grey-wedge type of photometer, which has been developed experimentally during the course of the work on hæmoglobin estimation. This last instrument, after several structural modifications, now appears to be in a form suitable for routine use and manufacture.

The validity of the base-line determinations has already been discussed in previous papers in this series, and iron analysis has again been taken as the standard of reference. It appears to provide the point of least variation from the other quantitative determinations which, in this instance, have involved several different derivatives of hæmoglobin. It will be seen that hæmoglobin mass as determined by iron analysis is very close to that derived by carbon-monoxide capacity after preliminary reduction, whereas oxygen-capacity estimations give consistently lower figures. It is reasonable to accept these two higher estimations as being the nearer to the true figure.

The variations of the results by the colorimetric and photometric methods have been calculated from the standard deviation of the ratios of observers' results to iron content of the blood samples used. Several points of interest arise regarding these estimates of reliability. The first is that, despite its simplicity, the neutral grey-wedge photometer gives results that are generally as good as those of the more elaborate and expensive instruments. Secondly, in these experiments the single-cell photo-electric colorimeter has proved more reliable than the more complicated two-celled absorptiometer. Thirdly, as regards the suitability of the various hæmoglobin derivatives for visual colorimetric or photometric estimation, it appears that oxyhæmoglobin and cyanhæmatin give the least variable results on the whole. Acid and alkaline hæmatin are inferior, though alkaline hæmatin gives good results when used in photo-electric instruments. In view of the disadvantage of cyanhæmatin for general routine use, because of the cyanide used, oxyhæmoglobin appears to us to be the derivative of choice for the neutral grey-wedge photometer. It not only gives good results but also is the simplest pigment to prepare.

Estimates of the reliability of the different methods, when used in different laboratories, are fairly consistent, apart from an occasional discrepancy. There seems, however, to be a curious difference between the results on blood samples from males as opposed to females. The latter show a greater over-all variation, particularly with certain pigments, such as acid hæmatin. No reason for this can at present be given.

The constancy of the relationship between hæmoglobin concentration and instrumental reading in the case of the grey-wedge photometer indicates the practicability of calibrating the scale of the instrument so that hæmoglobin values may be directly obtained. Further information on this point is in course of preparation.

It seems, then, that the grey-wedge photometer is capable of accurate results when enough readings are obtained by several observers. To be satisfactory in use, it is essential that the scatter between the results of different observers, each taking only a few readings, should be small. This point was covered by Macfarlane et al. (1948), who showed that this scatter was, at least when using oxyhæmoglobin, smaller than that of any of the hæmoglobinometers tested. It is therefore considered that the grey-wedge photometer should provide a convenient clinical hæmoglobinometer of considerable accuracy.

SUMMARY

The results of experiments to test the accuracy of precise colorimetric methods of estimating hæmoglobin are described.

Samples of normal blood from 11 male and 10 female adults were used.

Tests of six hæmoglobin derivatives indicate that oxyhæmoglobin and cyanhæmatin give the most accurate results. The performance of a new neutral grey-wedge photometer of simple construction compares favourably with that of standard photo-electric and visual instruments.

This investigation has been carried out for the Medical Research Council's subcommittee on analytical methods. The expenses incurred were partly defrayed by a grant from the Medical Research Council, to whom grateful acknowledgment is made. Our thanks are due to Sir Charles Harington, F.R.S., chairman of the subcommittee on analytical methods, for much valuable advice; and Miss K. Glaser, Mr. A. F. Hoffler, Miss P. Quelch, Mr. W. Weedon, Dr. Q. M. Gibson, Dr. A. Ferreira, Mr. D. B. Amos, Mrs. Olive Hayward, and many patient and willing observers for their valuable assistance. The colour and spectral-absorption measurements were carried out in the Light Division of the National Physical Laboratory on behalf of the Medical Research Council.

REFERENCES

Delory, G. E. (1943) *Analyst*, **68**, 5.
Donaldson, R., Harding, H. G. W., Wright, G. P. (1943) *J. Path. Bact.* **55**, 205.
Hüffner, G. (1894) *Arch. Anat. Physiol., Lpz.* p. 130.
King, E. J. (1942) *Lancet*, i, 511.
— (1947) *Biochem. J.* **41**, suppl. 32.
— Gilchrist, M. (1947) *Lancet*, ii, 201.
— — Delory, G. E. (1944) *Ibid*, i, 239.
— — Wootton, I. D. P., O'Brien, J. R. P., Jope, H. M., Quelch, P. E., Peterson, J. M., Strangeways, D. H., Ramsay, W. N. M. (1948) *Ibid*, i, 478.
— Haslewood, G. A. D., Delory, G. E. (1937) *Ibid*, i, 886.
Klumpp, T. G. (1934) *J. biol. Chem.* **107**, 213.
Macfarlane, R. G. (1945) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 252.
— King, E. J., Wootton, I. D. P., Gilchrist, M. (1948) *Lancet*, i, 282.
Peters, J. P., Van Slyke, D. D. (1930) Quantitative Clinical Chemistry. London.
Van Slyke, D. D., Neill, J. M. (1924) *J. biol. Chem.* **61**, 523.

"... At hospital we see large numbers of physicians and surgeons and regard illness as being natural to everybody. We fail to realise how ill-health strikes an ordinary family and there is a tendency to grow callous. ... The average patient goes into hospital once or twice in a lifetime and you arrive at the apex of the crisis of their life. Many patients are full of fear when going into hospital and we may find this difficult to understand; most patients know nothing of hospitals except perhaps that their mother or father died there. ... It is only by having an intense interest in the patients you handle that gradually you acquire the ability to assess the degree of illness. ... The more interested we are in people the more efficient we shall be in judging their state of health and their mentality. People can always be managed more efficiently if you know something about them. ..."—Dr. HORACE JOULES, addressing the Institute of Certified Ambulance Personnel, March 24, 1948.

Digitized by Google

UNEXPLAINED THROMBOSIS OF THE INTERNAL CAROTID ARTERY

H. R. I. WOLFE
M.B. Lond., F.R.C.S.
SENIOR ASSISTANT, SURGICAL UNIT, WELSH NATIONAL SCHOOL OF MEDICINE, ROYAL INFIRMARY, CARDIFF

IN the following case the sudden onset of coarse neurological signs followed by eighteen months' gradual improvement suggested cerebral vascular disease, and arteriography demonstrated thrombosis of the internal carotid artery.

CASE-RECORD

A slightly built woman, aged 26, was admitted on Jan. 16, 1947, complaining of difficulty in speaking. There was nothing relevant in her family history. Since the age of 1 year she had been treated for a concomitant squint of the left eye. During a routine examination for this condition in 1939 it had been noted that, unknown to the patient, the eye had become blind. Apart from this she had been well until August, 1945.

On Aug. 13, 1945, while serving in the A.T.S., she had got up feeling perfectly well. After dressing she tried to move a large box, felt a sudden weakness in the right arm, and fell to the ground, without losing consciousness but unable to speak. She was taken to the casualty reception centre and put to bed. On that day she tried to write but was unable to find the words. At that time she began to have sharp stabbing left temporal headache, radiating to the frontal region. There was anorexia but no nausea or vomiting. On the third day she suddenly developed weakness in the right leg.

By the end of September, some six weeks after the original incident, she began to write and read, though she had difficulty in finding words when writing and in understanding words when reading. Power gradually returned to the right arm and leg, and by mid-October she was allowed up, and fourteen days later she could walk half a mile without distress. Though power returned to her right arm, she was unable to perform the finger-to-thumb test accurately with her right hand. By the end of October she had lost the distressing headaches which had come on intermittently during the previous two months. Improvement continued until December, 1945, when she was invalided from the Service.

After this there was gradual improvement in the aphasia. She still had difficulty in speaking owing to an inability to find words and remember them. Reading was also difficult, since she could not understand some of the words in the text, but the disability was much less than previously and gradually decreased. She was not troubled with further headaches, and there was only slight residual disability of the arm and leg. The right hand "felt clumsy" but she could do household duties, knit, sew, and write. If she walked much, her right foot also became clumsy.

Examination.—She was alert and coöperative and tended to make light of her illness. There was a moderate aphasia, with difficulty in finding words. She had difficulty also in understanding what was said. She could read and spell words from the text, but some of them she could not understand.

There was slight nystagmus, greater on looking to the right, and slight incoördination of the right arm, the finger-to-nose test being performed rather clumsily. Her gait was steady, and there was no sensory disturbance or loss of power in the limbs. The cranial nerves were normal. The tendon-jerks were present but perhaps a little more brisk on the right side, the abdominal reflexes were present in all quadrants, and the plantar response was flexor on both sides.

Hand movements at 3 ft. and light could only be appreciated by the left eye. The visual field in the right eye was full. The fundi of both eyes appeared normal, and no abnormality of either optic disc or of the vessels of the left eye was detected.

The heart was normal on both physical and electrocardiographic examination. Blood-pressure 116/70 mm. Hg. Pulsation was normal in the radial, anterior tibial, posterior tibial, and dorsalis pedis arteries. There was no evidence of temporal arteritis. There was no pulmonary lesion. The blood prothrombin-time was 90% of normal, and the Wassermann reaction negative.

Lumbar puncture produced clear watery fluid under a pressure of 125 mm. of water. The rise and fall of C.S.F. pressure on jugular compression was rather sluggish. C.S.F. normal on examination. Kahn test negative.

Radiography showed general thickening of the bones of the skull, particularly the inner table of the vault. The mastoid air cells and the sphenoidal and ethmoidal sinuses were normal. In the rest of the skeleton nothing abnormal was found, nor was there any calcification of blood-vessels.

Arteriography (Jan. 25, 1947).—Exposure of the left carotid vessels for arteriography showed feeble pulsation in the external carotid, but the internal carotid was pulseless. Arteriography revealed an occlusion of the internal carotid about 2 cm. above the bifurcation of the common carotid artery (see figure). Periarterial stripping was performed at the bifurcation.

Electro-encephalography (Oct. 16, 1947) confirmed the site of the brain lesion.

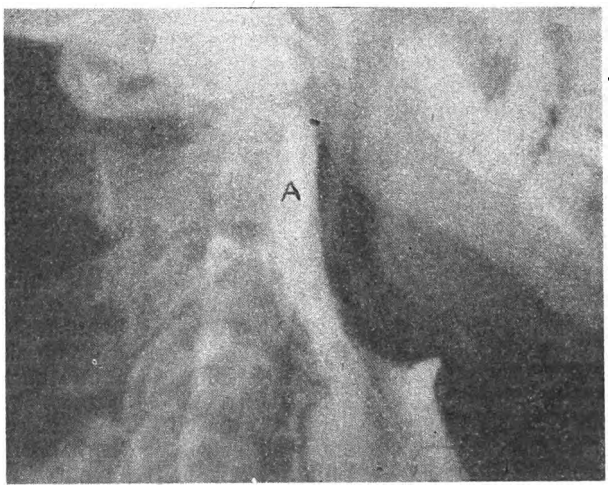
Progress.—Convalescence was uneventful. Eight months later, on Oct. 27, 1947, she was readmitted to hospital because she had become dull and apathetic, lacked initiative, and was careless of her appearance and bodily hygiene. Pneumo-encephalography showed much cerebral atrophy and asymmetry of the ventricles.

Operation (Nov. 8, 1947).—Under general anæsthesia a left superior cervical ganglionectomy was performed, and the left external and internal carotid arteries were divided between ligatures 1 cm. above and below the bifurcation of the common carotid artery. The diameter of the internal carotid artery was much reduced, and its peripheral portion appeared to be obliterated, its lumen being occluded by a firm white thrombus extending downwards into the common carotid artery and upwards into the external carotid artery for a few millimetres, partially occluding the lumina of both vessels.

Microscopical Findings.—A little proximal to the bifurcation of the common carotid artery organised thrombus filled most of the original lumen, leaving irregular channels containing fluid blood. The thrombus was attached to the intima over half the circumference of the vessel, with several gaps where fluid blood was in contact with the intima. The media was practically normal, with no obvious degenerative or inflammatory change. Close to the bifurcation of the common carotid artery the state of the external carotid artery resembled that of the common carotid artery, but the internal carotid artery had been completely thrombosed and recanalised, after which a further thrombosis had developed in one of the newly formed lumina. The media of this vessel was thin, appeared degenerate, and was penetrated by small vessels running from the perivascular region to the organised thrombus. There was only a slight inflammatory cellular infiltration in the vessel and surrounding tissues.

Further distally the external carotid artery had progressively less of its lumen occupied by the organised thrombus, whereas the internal carotid artery was almost completely obliterated throughout the length examined.

Progress.—Convalescence was uneventful, but up to Sept. 6, 1948, there had been no demonstrable improvement in the patient since operation.



Angiogram showing occlusion of left internal carotid artery: A, cone-shaped termination of opaque 'Thorotrast' column just below atlas.

Digitized by Google

DISCUSSION

The history is characterised by the sudden onset of aphasia and weakness of the right arm followed three days later by weakness of the right leg and a subsequent gradual but incomplete recovery. Eighteen months after the original incident there was slight mental deterioration, aphasia, and remnants of a right-sided hemiplegia. Arteriography showed thrombosis of the left internal carotid artery. Subsequently a segment of the common carotid, external carotid, and internal carotid arteries on the left side was excised. The internal carotid artery appeared to be completely occluded by a thrombus extending a short distance into the common and external carotid arteries, which were partially occluded. Microscopically the walls of the common and external carotid arteries were not obviously diseased, but there was degeneration in the media of the internal carotid artery and a slight inflammatory cellular infiltration of that vessel and its perivascular tissue. The structure of the thrombus in the internal carotid artery showed that complete thrombosis had been followed by recanalisation and subsequent further thrombosis. The neurological signs suggest that extension of the clot distally took place on the third day, arterial spasm being unlikely in view of this latent period. Almost complete recovery from the hemiplegia suggests recanalisation.

The demonstrable vascular occlusion was presumably responsible for the neurological symptoms, but the cause of the thrombosis is more obscure. There was no evidence of injury whereby the vessel might have been damaged. Minute injuries due to muscular exertion, or abnormally developed fascial bands, were thought by some a possible cause of "idiopathic" thrombosis in the femoral and popliteal arteries of young men in the Services during the war. The bifurcation of the common carotid artery in the present case was abnormally high and may have rendered the internal carotid artery liable to such an injury and subsequent thrombosis. This hypothesis is only speculative, since the evidence for holding normal anatomical structures responsible for "idiopathic" thrombosis is not strong.

There was no evidence of an inflammatory process or of a tumour in either the bone or the soft tissues in relation to the artery, and nothing to indicate syphilis. Embolism is unlikely, since this girl had no sign of either valvular disease or myocardial damage. Repeated observations of the blood-pressure (116/70) did not show any significant fluctuations, and in the absence of either palpable or radiological evidence of arteriosclerosis there is little to support the assumption that either hypertensive arteriosclerosis or a sudden drop in blood-pressure was responsible.

Radiography of the skull showed a general thickening, particularly of the inner table of the vault. One reported case of thrombosis of the internal carotid artery subsequently developed Christian-Schüller's disease (Andrell 1943). Though the radiological change in the skull might be interpreted as that following spontaneous healing of a xanthomatous lesion, this diagnosis appears unlikely, since there was neither a previous history pointing to skeletal xanthomatosis nor other evidence of this condition.

It is unfortunate that there is no record of an examination of the C.S.F. when this young woman was first taken ill, for it is just possible that a "berry" aneurysm of the circle of Willis was responsible for the thrombosis. In the necropsy records of the Cardiff Royal Infirmary there is an account of a fatal subarachnoid hæmorrhage due to a "berry" aneurysm at the termination of the internal carotid; the lumen of the vessel was partially occluded by an extension of clot from the aneurysmal sac. This is the only one of 35 cases in which partial occlusion was reported, and I have been unable to find a published report of a case in which complete occlusion was found.

Thrombo-angiitis obliterans, a progressive inflammatory lesion of the arteries with secondary thrombosis, is a generalised disease of the blood-vessels and may occur in any organ. Thrombosis of one internal carotid artery in association with cerebral thrombo-angiitis has been observed (Sorgo 1939, Antoni 1941, Sunder-Plassman 1941, Andrell 1943, Davies and Perret 1947). Cerebral thrombo-angiitis tends to involve the smaller vessels over the hemisphere, and the affected cortex shows areas of softening, glial scar tissue, and normal cortex. Pneumo-encephalography in the present case showed changes due to atrophy. Though cerebral thrombo-angiitis is thought to be responsible for the thrombosis in this case, in the absence of clinical signs of more widespread vascular disease or a systematic examination of the vascular system which could only be done at necropsy, the diagnosis cannot be regarded as established.

Previously Recorded Cases

Numerous cases of thrombosis of the carotid vessels have been published. Thrombosis of the common carotid artery is rare, and bilateral thrombosis even rarer; Frøvig (1946), who reported a case, found reports of only 11 similar cases. Most of the reports concern obliteration of the internal carotid artery. I have found reports of 32 cases (Lohr 1936, Moniz 1937, Shimidzu 1937, Chao et al. 1938, Riechert 1938, Siegert 1938, Sorgo 1939, Andrell 1943) in which thrombosis was recognised arteriographically. In these cases and in the present case the age and sex of the patients and the side on which the lesion occurred were as follows:

Age (decade) ..	3rd	4th	5th	6th	7th	8th
No. of patients..	1	6	4	11	10	1

Males 26; females 7.
Left side 23: right side 10.

Arteriosclerosis is thought by Andrell (1943) to be responsible for the thrombosis in most cases. Material from 6 of the 32 cases previously described was examined pathologically. In 1 fatal case, Antoni (1941) found changes in the cerebral vessels due to thrombo-angiitis. In 5 a segment of the occluded vessel showed that arteriosclerosis had caused the thrombosis in 3, and thrombo-angiitis in 2. In the remaining 17 cases arteriosclerosis was diagnosed in 7, no cause could be found for the vascular pathology in 7, 1 was thought to be due to thrombo-angiitis, 1 was associated with syphilis, and 1 was followed by Christian-Schüller's disease.

Diagnosis

The diagnosis is difficult. The duration of symptoms and their transient character in the early stages suggest cerebral vascular disease. Pneumo-encephalography will provide evidence of cerebral atrophy. Precise diagnosis requires arteriography.

In a little over half the cases the disease pursues a chronically progressive course, and an initial stage characterised by transient cerebral symptoms can be recognised. Premonitory attacks of headache are the most constant. The headache, localised to the side of the lesion, transient, and of short duration, may occur periodically for years before the manifestation of other symptoms. Occasionally it is associated with visual disturbances or with neurasthenic symptoms. Hemiparesis, hemiparæsthesia, speech difficulties, and transient blindness have been reported. These symptoms, which develop in attacks of short duration and subside rapidly, are followed after months or years by more severe attacks, the last at times being apoplectic. As in the cases here described, this stage may be absent and the first sign of the disease be the acute onset of gross neurological symptoms, the commonest being hemiplegia involving chiefly the arm. Initially this may be transient

Digitized by Google

(9 cases), later becoming irreversible (23 cases), or it may be irreversible from the beginning. In some cases the paresis at its onset is not pronounced, clumsiness of the extremity only being observed. Hemianæsthesia (3 cases), hemiparæsthesia (2 cases), and paræsthesia of the contralateral arm (1 case) have also been recognised.

In 6 of the cases recorded by Andrell (1943) alterations in the left internal carotid artery were demonstrated, and all showed aphasia. Though the aphasia, apart from weakness of the right lower facial branch, was unassociated with other neurological signs in 1 case, the remainder were associated with hemiplegia of various degrees of severity. The aphasia preceded the onset of paralysis in 2 cases, occurred at the same time in 2, and followed the paralysis in 2. Aphasic troubles in a right-handed person with thrombosis of the right internal carotid artery have also been observed (Siegert 1938, Sorgo 1939, Andrell 1943). The facial was the most often involved of the cranial nerves, paresis being reported in 20 cases. Paresis of the spinal accessory (3 cases), the hypoglossal (4 cases), and the abducens (1 case) was less common. Symptoms referable to the distribution of the opthalmic artery, thrombosis of the central retinal artery, attacks of transient blindness (Andrell 1943), inequality of the pupils with miosis on the side of the thrombosed vessel (Siegert 1938, Sorgo 1939), and alterations in the eye suggesting stasis (Moniz 1937, Riechert 1938, Sorgo 1939) were less frequent.

Treatment

Thrombosis of the internal carotid artery seems to be uninfluenced by treatment. Surgical treatment has been directed to the relief of spasm of the cerebral vessels. Periarterial sympathectomy, excision of the thrombosed part of the artery, extirpation of the cervical sympathetic, and resection of the common carotid artery with the adjoining portion of the external and internal carotid arteries have all been tried. Of the 33 cases of thrombosis of the internal carotid artery diagnosed by arteriography there has been a gradual amelioration of symptoms in about half, in 3 after excision of a segment of the thrombosed artery. There were 7 deaths, 2 of these being due to intercurrent infection. Neither heparin nor dicoumarol seems to have been used in these cases. The history of the present case indicates that on the third day there was a spread of the thrombosis. If the vascular nature of the lesion could have been recognised three days earlier, alteration of the clotting-time might have prevented further extension of the thrombus. This patient remains under observation, but treatment appears to have had little effect on the course of the disease.

SUMMARY

A case of thrombosis of the left internal carotid artery in a young woman is reported. The pathology, diagnosis, and treatment of 32 previously reported cases diagnosed by arteriography are commented on.

I am indebted to Prof. F. L. Golla and Mr. Grey Walter, of the Burden Neurological Institute, for the electro-encephalographic reports; Prof. J. Gough, of the pathological department of the Welsh National School of Medicine, for the pathological reports; and Prof. Lambert Rogers, director of the surgical unit, for advice with this case.

REFERENCES

Andrell, P. O. (1943) *Acta med. scand.* **114**, 336.
Antoni, N. (1941) *Ibid*, **108**, 502.
Chao, W. H., Kwan, S. T., Lyman, R. S., Loucks, H. H. (1938) *Arch. Surg.* 37, 100.
Davies, L., Perret, G. (1947) *Brit. J. Surg.* **34**, 307.
Frøvig, A. G. (1946) *Acta psychiat., Kbh*, suppl. 39.
Lohr, W. (1936) *Zbl. Chir.* **63**, 2593.
Moniz, E. (1937) *Pr. méd.* **45**, 977.
Riechert, T. (1938) *Nervenarzt*, **11**, 290.
Shimidzu, K. (1937) *Arch. klin. Chir.* **188**, 295.
Siegert, P. (1938) *Arch. Ophthal., N.Y.* **138**, 798.
Sorgo, W. (1939) cited by Andrell (1943).
Sunder-Plassman, P. (1941) *Dtsch. Z. Chir.* **254**, 463.

INTESTINAL OBSTRUCTION FROM FIBROUS STRICTURE

FOLLOWING STRANGULATED HERNIA

P. KONSTAM
F.R.C.S.E.
LATE RESIDENT SURGICAL OFFICER, CRUMPSALL HOSPITAL, MANCHESTER

Barry described three cases of this rare condition and fully reviewed published cases.[1] Two more cases came under my care within three weeks of each other.

Case 1.—A man, aged 69, was admitted to hospital on Sept. 22, 1945, with the history that a large right inguinal hernia, which he had had for many years and for which he wore a truss, had become strangulated and been reduced by taxis by his own doctor before admission. A large tender right inguinal hernia was found, not completely reducible, and with no sign of strangulation. The patient was admitted for observation. Pain and vomiting recurred, and operation was undertaken.

First Operation (Oct. 2).—A coil of ileum 4 in. long was found fixed in the hernial sac; there were well-developed truss adhesions. No definite evidence was found of interference with the blood-supply to the gut which was therefore returned to the abdominal cavity. The hernia was repaired.

Progress.—On Oct. 8 the patient began to vomit and complain of lower abdominal pain. There was no distension of the abdomen, and flatus was passed. On Oct. 13 there was severe colicky central abdominal pain and the patient vomited several times. His bowels had not been open for two days. There was some central distension of the abdomen. The condition settled with the passage of Ryle's tube and with gastric suction. The patient was discharged on Oct. 10. He was readmitted on Oct. 30 with a history of pain across the abdomen and in the back for ten days and constipation for two days. There had been no vomiting. His tongue was furred, and his temperature and pulse-rate were normal. A step-ladder pattern of small gut coils was visible. There was much distension of the central abdomen, with tinkling peristaltic sounds. Subacute intestinal obstruction in the region of the terminal ileum was diagnosed.

Second Operation.—The ileum was much distended and contained gas and fluid. A segment just proximal to the ileocæcal junction was narrowed and indurated, with two large glands in its mesentery. The terminal section of the ileum was normal. An ileo-transverse colostomy was made.

The patient was discharged on Nov. 23 after an uneventful recovery. Seen as an outpatient on Jan. 15, 1946, he said he had had diarrhœa for six weeks after discharge but was now well.

Case 2.—A man, aged 60, was admitted to hospital on Oct. 10, 1945, with eight hours' history of colicky abdominal pain. He had vomited much brown material. His bowels had been open the day before. He had had a right femoral hernia for eight years. On admission his pulse and temperature were normal, and his tongue dry. His abdomen was a little distended, with loud tinkling noises on auscultation.

First Operation.—The femoral sac was opened and found to contain 6 in. of strangulated but viable small gut, some omentum, and some plum-coloured fluid. The contents of the sac were reduced and the hernia repaired.

Progress.—On Oct. 24 the patient complained of colicky central abdominal pain and vomited some bile. His abdomen was not distended. On Nov. 6 there were further attacks of intestinal colic, with loose motions. An anteroposterior radiogram of the abdomen did not justify a diagnosis of obstruction. On Nov. 7 the patient's temperature was 100°F and his abdomen soft. Stools showed no occult blood or pathogenic organisms. On Nov. 15 there was well-marked abdominal distension, with pain more severe. Audible peristalsis suggested obstruction of small gut.

Second Operation.—The ileum about 5 in. from the ileocæcal valve was indurated and narrow, like a rubber tube. The gut above the obstruction was much distended. The constricted segment was 2 in. long and $^3/_4$ in. in diameter, and tapered towards the ileocæcal valve. A constriction ring was still present. The related mesentery showed several

1. Barry, H. C. *Brit. J. Surg.* 1942, 30, 64.

Digitized by Google

strands of fibrous tissue, and there were several large hard mesenteric glands, one of which was taken for biopsy. The affected bowel was short-circuited by an ileo-ileostomy. The gland showed changes due to pyogenic infection, and when cultured yielded a pure growth of *Staph. pyogenes*.

The patient made an uninterrupted recovery.

COMMENTS

These patients were 69 and 60 years old. In one case signs of obstruction developed 18 days after reduction of a strangulated right inguinal hernia, and in the other between 14 and 35 days after operative reduction of a strangulated right femoral hernia. In one case necrosis of the mucosa gave rise to diarrhœa 21 days after strangulation; the diarrhœa in the other case was possibly a result of ileo-transverse colostomy. Growth of *Staph. pyogenes* from a mesenteric gland in the second case suggests that damage to the mucosa allowed the organisms to penetrate to the deeper tissues of the bowel.

Neither case showed intestinal hæmorrhage. The diagnosis of Crohn's disease was ruled out by the histories. Both patients did well after a simple short circuit of the affected part of the ileum.

I am indebted to Dr. W. Ramsay, medical superintendent of Crumpsall Hospital, Manchester, for permission to publish these cases, and to Dr. G. Stewart Smith for the pathological report.

Preliminary Communication

TETRAETHYLAMMONIUM BROMIDE IN RENAL CORTICAL ISCHÆMIA

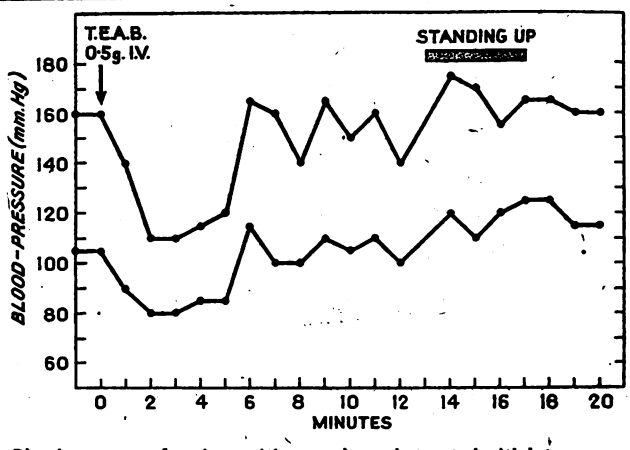
TRUETA et al.[1] have presented a new picture of the circulating pathways in the kidney and emphasised its importance in the pathogenesis of various clinical states. We have confirmed their observations and studied the effect of tetraethylammonium bromide on the renal circulation, especially as regards its possible application to the prevention and treatment of toxæmia of pregnancy and other conditions.

Experiments were first made to inject the normal renal circulation. Rabbits of about 2 kg. body-weight were injected with indian ink by the technique which is advocated by Trueta et al. and very satisfactory naked-eye appearances were produced. The technique is as follows:

The mesenteric vessels are ligated, and a hypodermic needle is inserted into the abdominal aorta just above the bifurcation and directed against the blood-stream. The aorta is next tied round the needle. 'Mandarin' indian ink diluted 1 in 3 is injected so that the head of the injected mass is kept just above the origin of the renal arteries. This point can be found by observing the colour of the left suprarenal gland, which becomes and remains black while the ink is kept at the correct level, but rapidly becomes pale if there is insufficient ink in the aorta.

The normal kidney injected in this way rapidly becomes uniformly black after 3 or 4 ml. of ink has been injected. The renal pedicle is next clamped, and the kidney removed and fixed in formalin for twelve hours, after which it is sectioned and photographed. The cortex of the normal kidney appears uniformly black to the naked eye.

In other rabbits faradic stimulation was applied to the left splanchnic nerve for 10 min. The surface of the kidney became pale and, when 3–4 ml. of indian ink had been injected, appeared irregularly red and black, showing that some areas of the cortex were ischæmic. If 20 ml. of ink was injected over a longer period, the cortex became uniformly black, and a cut section showed ink distributed throughout cortex and medulla, suggesting that the vascular spasm could be overcome by increased pressure in the renal artery.



Blood-pressure of patient with pre-eclampsia treated with intravenous T.E.A.B.

Effect of Crushing a Limb

Observations were next made to confirm the effect of crushing the limb. The rabbit was anæsthetised with intravenous pentobarbitone sodium supplemented with open ether as required. A wire tourniquet was applied to the left hind limb sufficiently tight to occlude the circulation and crush the muscles without cutting through them. The tourniquet was left on for 4½–5 hours, after which the same injection technique was used. It was found, as Trueta et al. noted, that the kidneys were injected unevenly, the left being more patchy than the right.

Effect of Splanchnic Paralysis

Trueta et al. state that the vascular change in the kidney depends on the integrity of the splanchnic nerve, and that after section of the nerve the renal cortical shunt cannot be produced. No attempt was made to confirm this particular observation directly, since we were interested in a more rapid method of altering the renal circulation—by the use of the rapidly acting sympathetic paralytic drug tetraethylammonium bromide (T.E.A.B.). This was given in 10% solution by intramuscular injection, the dose being 0·2 ml. per kg. of body-weight.

The rabbit was anæsthetised as before, and intramuscular T.E.A.B. was given. A tourniquet was next applied as before for 4½ hours, and indian ink was injected. The injection pattern was completely uniform and identical with that of a normal kidney. This experiment was repeated in 6 rabbits with similar results, suggesting that an adequate dose of T.E.A.B., given before the application of the effective stimulus, was as effective as splanchnic section in preventing the renal cortical ischæmia.

In clinical practice, however, such conditions are unlikely to arise, and it seemed more important to determine whether T.E.A.B. would be as effective if given some time after the effective stimulus. The experiments were therefore repeated, and an intramuscular injection of T.E.A.B. was given in different rabbits one, two, or three hours after the application of the tourniquet. In the rabbits in which only one or two hours had elapsed between the stimulus and the injection of T.E.A.B. the renal circulatory pattern was normal, whereas in the rabbits in which a longer period had elapsed there was usually cortical ischæmia. It therefore seemed possible to prevent the development of renal cortical ischæmia by injecting T.E.A.B. after the application of the effective stimulus, and despite the persistence of that stimulus, provided the interval was not too long.

1. Trueta, J., Barclay, A. E., Franklin, K. J., Daniel, P. M., Prichard, M. M. L. Studies of the Renal Circulation. Oxford, 1947.

Digitized by Google

CLINICAL APPLICATION

These observations seem important in several clinical conditions in which renal cortical ischæmia is probably the underlying pathogenic factor—namely, essential hypertension, pre-eclampsia, traumatic anuria, and reflex anuria. For some time we have been interested in the possible relationship between toxæmia of pregnancy and essential hypertension, for the best results of splanchnicectomy for hypertension seem to be obtained in patients whose disease originates in pre-eclampsia. The clinical syndromes of pre-eclampsia and of eclampsia resemble that of malignant hypertension so closely that it is difficult to believe that they have not a common origin in renal cortical ischæmia, and that it is possibly a hereditary factor which makes malignant hypertension permanent, whereas pre-eclampsia and eclampsia improve after the termination of the pregnancy. Further, it has been shown [2] that renin can be detected in the blood of patients with pre-eclampsia and in those with eclampsia as well as in those with malignant hypertension. We therefore turned our attention to patients with pre-eclampsia. It was found that by blocking both splanchnic nerves with procaine the blood-pressure could always be reduced to a normal level. The blood-pressures before and after splanchnic block in five consecutive patients were as follows:

	Blood-pressure (mm. Hg)				
Before ..	170/105	150/95	190/100	160/90	195/115
After ..	120/75	100/60	130/70	110/70	170/100

An attempt was made to render the splanchnic block permanent, but alcohol was unsuitable because of the difficulty of placing it sufficiently accurately and because it was invariably followed by severe intercostal neuritis, whereas 'Proctocaine' was unsuitable because it diffused so rapidly. When proctocaine, rendered radio-opaque by the addition of a little iodised oil, was injected at the level of the 11th and 12th dorsal vertebræ, it tracked as far as the 5th lumbar vertebra in forty-eight hours.

We therefore tried T.E.A.B. and found that an intravenous injection of 0·5 g. usually produced a well-marked though temporary fall in blood-pressure (see figure). Postural hypotension was usually, though not invariably, present for about 15 min. We then used T.E.A.B. by intramuscular injection to obtain a prolonged effect, giving 1 g. six-hourly for twenty-four hours followed by 1 g. three-hourly for twenty-four hours. The initial results were disappointing. Only four cases have so far been treated, but in the last case the blood-pressure fell to normal twenty-four hours after the last injection and remained so for about seven days. Probably, therefore, intramuscular T.E.A.B. must be given for a much longer time to have the desired effect.

COMMENTS

T.E.A.B. may be the answer to the problem of treatment of several closely related syndromes in which the renal circulation is primarily at fault. Repeated large doses of T.E.A.B. deserve a trial in the prevention and treatment of such conditions as concealed accidental hæmorrhage, crush injuries, and possibly blackwater fever, all of which may be accompanied by oliguria due to renal cortical ischæmia.

This work, interrupted through unforeseen circumstances, is obviously incomplete, but it is hoped that other workers may give the method a wider trial.

SUMMARY

The work of Trueta et al.[1] on the presence of two alternative vascular pathways through the kidney has been confirmed by repetition of their experiments.

The effect of tetraethylammonium bromide on the renal circulation has been studied in rabbits, and an intramuscular dose of 0·2 ml. of a 10% solution per kg. of body-weight has been shown to prevent cortical ischæmia.

Intramuscular doses of 1 g. six-hourly for twenty-four hours, followed by 1 g. three-hourly for twenty-four hours, caused the blood-pressure to return to normal for seven days in 1 out of 4 cases of pre-eclampsia.

It is suggested that a longer period of this treatment may have the desired effect in a greater proportion of cases.

I wish to thank my colleagues Prof. T. N. A. Jeffcoate, Mr. St. George Wilson, and others for allowing me to study patients with pre-eclampsia admitted under their care. We are grateful to Pharmaceutical Specialities (May and Baker) Ltd. for the tetraethylammonium bromide used in the animal experiments.

FRANCIS E. STOCK
F.R.C.S.

Department of Surgery, University of Liverpool.

2. Dexter, L., Haynes, F. W. *Proc. Soc. exp. Biol., N.Y.* 1944, 55, 288.

Reviews of Books

Surgery of Abdominal Hernia

GEORGE B. MAIR, M.D., F.R.F.P.S., F.R.C.S.E., surgeon, Law Junction Hospital, Lanarkshire. London: E. Arnold. 1948. Pp. 408. 25*s*.

THIS book really consists of two parts—a monograph on the use of whole-skin grafts in hernia repair, and, round this, a general treatise on hernia. The first, which conveys the author's views and experience, is the best; the remainder is painstaking and impersonal, and (as always when a writer is editing the views of others rather than stating his own) is overloaded with quotations from obscure surgeons supporting bizarre theories. Lytle's masterly description of the internal ring, which agrees with those of Astley Cooper and Hesselbach, is ignored, and we find in its place a circular sphincter of muscle which was apparently seen by someone in 1929.

Mr. Mair's use of the purely Scottish word "outwith" goes with a clear style and forthright manner, and his account of his own work with whole skin will interest most surgeons. A record of 140 indirect herniæ operated on by this method with only 1 recurrence after a year, and of 40 direct herniæ similarly treated with no recurrence after three years, is one of which anyone might be proud. But while the author's advocacy and his results will persuade many surgeons to try his technique, its ultimate survival will depend on the results that others get. It is clear that the graft is eventually converted into, or replaced by, a firm sheet of fibrous tissue, but only after a battle lasting six months in which fibroblasts, foamy cells, and giant cells struggle over dead epidermis, hair fragments, desquamated elastic fibres, clumps of bacteria, and small abscesses. Clinically these struggles seem to be indicated by a local reaction greater and more prolonged than usual.

The book usefully fills a place. It will be consulted by those who want a clear account of the whole-skin graft method of repair, and by those who seek information and references in relation to rare or atypical herniæ.

Disorders of Sex and Reproduction

A. P. PILLAY, M.B. London: H. K. Lewis. 1948. Pp. 299. 18*s*.

IN former days sexual difficulties and impaired fertility were generally neglected by doctors, mainly because they were not lethal; and now their treatment has passed into the hands of the gynæcologist, the urologist, the endocrinologist, and the psychologist. This has the disadvantage that patients have to be referred from one doctor to another during the course of their treatment, and Dr. Pillay argues that it would be better for them to be under the care of a single specialist in "sexology." He has devoted himself for many years to the diagnosis and treatment of sexual and reproductive disorders in both sexes, and this book is the fruit of his varied professional experience. It gives a balanced view of forms of illness which often cause great mental distress, even though they are not the cause of serious

Digitized by Google

ill health, and it shows that in their management psychotherapy has a very important place. Even if he is not competent to conduct a deep analysis, the doctor who treats such troubles must be able to deal with his patients' more obvious fears and inhibitions. Dr. Pillay gives interesting case-reports, in simple language, which illustrate how this may be done. His book also provides a good survey of sexological literature, and his final chapter deals with the thorny subject of artificial insemination. A few more illustrations would have been helpful.

Advances in Enzymology and Related Subjects of Biochemistry

Vol. VIII. Editor: F. F. NORD, Fordham University, New York. New York and London: Interscience Publishers. 1948. Pp. 538. 48*s*.

ANOTHER volume has been added to this annual publication, which first appeared early in the war, and followed the *Ergebnisse der Enzymforschung*, published in Germany before 1940. The series is valuable to both research-worker and university teacher. The articles in volume VIII range from a highly specialised review on the katabolism of fatty acids to a general survey of the functions of cytoplasm. Heidelberger and Mayer's review of recent American work on complement emphasises the importance of preliminary selection and preparation of the analytical tools to be used in an investigation. Chaikoff and Entenman discuss pancreatic factors capable of preventing fatty infiltration of the liver in depancreatised insulin-treated animals. There seem to be several of them, two—choline and methionine—being dietary and interrelated, while one, or possibly two, are unknown substances. A statistical study of the earlier results of this work would have been welcome, since the great variation, from animal to animal, in the degree of fatty infiltration of the liver makes some of the later results difficult to assess.

It is in keeping with the world fat-shortage that four out of ten reviews in the book should deal with fat metabolism. Breusch's review of the breakdown of fatty acids in the body is well documented, and capably summarised. Perhaps the most challenging review is that by Ludwik Monné on the cytoplasm, and the suggestion that memory, intuition, and fantasy are but expressions of the synthesis of specific proteins should not be taken too seriously.

Emergencies in Medical Practice

Editor: C. ALLAN BIRCH, M.D., F.R.C.P., physician, Chase Farm Hospital, Enfield. Edinburgh: E. & S. Livingstone. 1948. Pp. 468. 25*s*.

THIS is not a pocket companion-in-trouble for the practitioner faced with an emergency. It is much too diffuse for that. Some of the sections—e.g., that by Dr. Avery Jones on the treatment of gastroduodenal hæmorrhage—are models of clear straightforward help in an emergency; and the addresses and telephone numbers for obtaining lesser-known remedies, and for contacting the right administrative authorities, are an excellent feature. But details of the number of thunderstorms on the earth per diem, a description of the first successful pulmonary embolectomy performed in England, and a story about fish stings, though interesting, would exasperate a doctor faced with a crisis. Also, though some of the illustrations, particularly those drawn by Mrs. Birch, are excellent, many are of little practical value. The portraits of three South African scorpions merely add an extra page.

The pocket companion-in-trouble, however, is not the only kind of book on emergencies: there is also the armchair treatise to be read and memorised in preparation for later contingencies. It would, indeed, be quite simple to settle down to read and make notes from this book, which would prepare the doctor for almost any eventuality. But if it is intended for this purpose, it is perhaps a pity that it is not properly provided with references.

It is a matter of opinion what constitutes an emergency. Dr. Birch in his preface defines it as anything that calls for immediate action, without even the refinements of exact diagnosis. But the body of the book treats as an emergency any disorder for which it would be as well to do something in the next couple of days or so. A retroverted gravid uterus, a bedsore, a disease transmitted by blood-transfusion, polycythæmia, and hypochromic microcytic anæmia are hardly emergencies in the editor's sense; and surely acute gout, which is not mentioned, is more worthy of inclusion. Actually its scope is probably best explained by Dr. Birch's remark that he found that clear and concise instructions on what to do in the treatment of acute and urgent illnesses were scattered among the sections on general therapeutics in medical textbooks. In assembling such instructions under one cover he has produced a textbook of medical therapeutics arranged on symptomatic lines, and in the next edition it might be well to drop the emergency aspect of the title. More drastic editing would also be an advantage; for it is difficult to keep to a consistent pattern in a book with eighteen authors—as is seen by comparing the chapters on medical emergencies in obstetrics with the one on acute abdominal catastrophes. For a book of this kind, to be read quietly as a textbook, Prof. Robert Platt's remarkable chapter on emergencies in renal disease might well be taken as the pattern. The inclusion of chapters on medical emergencies at sea and in the air is original and useful.

Endocrinology of Neoplastic Diseases

A symposium by eighteen authors. Editors: G. H. TWOMBLY, M.D.; G. T. PACK, M.D. New York and London: Oxford University Press. 1947. Pp. 392. 60*s*.

THIS book is a good example of collective scientific literature. The reputation of its authors is a guarantee of the high standard of the work, and every reader can count on getting valuable instruction from it. By careful scrutiny a few lapses can be found: thus spontaneous uterine tumours in the rabbit are stated to be extremely rare, and on this incorrect opinion an important conclusion has been founded. (The fact is that spontaneous uterine tumours in the domestic rabbit are remarkably common.) Again, the assertion that castration and the administration of stilbœstrol "are opposite rather than similar forms of therapy" is questionable; and the old idea is advanced that the adrenal cortex is formed from juxtacapsular cells which gradually pass inward until their destruction and disappearance in the reticular zone—an account of adrenal development which in this unmodified form is not accepted by everyone.

The symposium as a whole is founded on fact; guesswork—that ever-present bugbear of medical literature—is nearly absent. The various articles are competently written; and the contribution by R. A. Moore in particular is an example of how a scientific paper ought to be presented. The references at the end of each chapter are copious and add much to the value of the book.

Diseases of the Chest (2nd ed. Edinburgh: E. & S. Livingstone. 1948. Pp. 541. 25*s*.).—The first edition of Dr. Robert Coope's book has been twice reprinted since it appeared in 1944. In this second edition he has modified the description of the anatomy of the bronchial tree to bring it into line with the work of Hoyle and Foster-Carter and of Brock. The book remains probably the best presentation of its subject in small compass.

Laboratory Diagnosis of Protozoan Disease (London: H. Kimpton. 1948. Pp. 384. 27*s*. 6*d*.).—In temperate climates there has been a substantial increase in the numbers of people harbouring the so-called tropical infections, many of which are protozoan or helminthic. Sometimes these infections persist for many years, or even for life, unless eradicated by specific treatment. Their detection is comparatively easy in skilled hands; but there is much ignorance of the methods of recovering, finding, and identifying the parasites. This book by Colonel Chas. Franklin Craig, of Tulane University, when published in 1942, was widely accepted as sound and authoritative—and the second brings it up to date. The work is confined to the protozoa, and includes detailed descriptions of new methods in diagnosis which have been developed during the war. It is clearly printed, well written and illustrated, and of convenient size. It can confidently be recommended as a bench companion to the clinical pathologist, and may be studied with profit by the physician called upon to deal with men or women returned from overseas.

Digitized by Google

47286a

TRADE MARK

'THEOGARDENAL'

BRAND

theobromine and phenobarbitone

tablets

The vaso-dilator and diuretic actions of theobromine and the sedative effect of phenobarbitone are combined in an effective synergistic form in 'Theogardenal'.

It is of great value in the symptomatic relief of hypertension. In therapeutic dosage it is non-toxic, has no cumulative effect and is well tolerated even when prescribed over lengthy periods.

tablets: *(theobromine gr. 5 and phenobarbitone gr. ½)*
Containers of 25, 100 and 500

manufactured by

MAY & BAKER LTD

distributors

PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD. DAGENHAM

LIKE EXPELLING WATER FROM A SPONGE

ŒDEMA due to cardiac failure

Control of œdema lightens the work of the failing heart. Digitalis and other cardiac tonics can again show beneficial action.

Using 'Salyrgan,' dropsical accumulations are rapidly drained from the tissues and œdema is kept at a minimum. The preparation may be administered either in ampoule or in pellet form.

'Salyrgan' is supplied in amps of 1 c.c. and 2 c.c. in boxes of 5, 25; and in pellets of 0.08g. in tubes of 20, bottles of 250.

'SALYRGAN'

TRADE MARK BRAND OF MERSALYL™

BAYER PRODUCTS LIMITED, AFRICA HOUSE, KINGSWAY, LONDON, W.C.2

Digitized by Google

The heart
that is ageing

In these days when increasing attention is being devoted to the care of the elderly, the use of certain xanthine derivatives has gained considerable favour for improving myocardial function and for patients whose coronaries are probably sclerotic or constricted. A useful representative of this group for routine treatment may be found in

Cardophylin

THEOPHYLLINE-ETHYLENEDIAMINE

VASODILATOR, DIURETIC & RESPIRATORY STIMULANT

●

Its use is indicated in Angina Pectoris, Coronary Thrombosis, Cheyne-Stokes Respiration, Oedema, and Bronchial Asthma.

Supplied in tablets for oral use, ampoules for intramuscular and intravenous injection and in suppositories.

SAMPLES AND LITERATURE ON REQUEST

Manufactured by WHIFFEN & SONS LTD.

Distributed by BRITISH CHEMICALS & BIOLOGICALS LTD. (Bengers-Genatosan Division), Loughborough

to whom all orders and enquiries should be sent

Digitized by Google

THE LANCET

LONDON: SATURDAY, OCT. 9, 1948

Under Tension

THE cause of the present international crisis, we are told, is the antagonism of democratic and totalitarian conceptions of government. Psychologically, the democratic and the totalitarian régimes represent two different types of adjustment to gregarious life; and each has a long history. What is the essential difference between them?

The two types of adjustment may be contrasted by reference to the old saying "It takes all sorts to make a world." Those who can accept this exacting notion are prepared to find satisfaction in the thought that others may be very unlike themselves and yet be worthy of respect and even affection. People with such an attitude of mind can tolerate, without undue strain, profound divergences of outlook in the world in which they live; indeed they may even experience a relief when there is not too much uniformity in the cultural pattern. To take an instance from the political field, His Majesty's Opposition is accorded almost as much respect as His Majesty's Government, for both are loyal to the Throne and both are made up of persons who represent the people; and when they are of almost equal power we have a feeling that our constitution is safe, since changes will not come at a speed we cannot check. Other instances in this country include the unembittered rivalry of religious groups, the general tolerance of agnosticism, the easy mixing of age-groups in the community, and, above all, the way in which ancient institutions are adapted to present purposes instead of being destroyed. The ideal democracy is based on a conviction that the fullest life is only to be found in a diversely constituted society. The totalitarian, on the other hand, holds that conflict of ideas within his nation or group is dangerous, and his remedy for internal tension is to induce everyone to think alike and behave alike. This attitude long antedates the Soviet and Nazi totalitarian states. In pre-revolutionary Russia it found expression in the oneness-of-mind which characterised the decisions of the village *mir*, in the religious notion of *sobornost* (a sort of pentecostal unifying inspiration of the whole congregation), and in political and religious self-abnegation. The readiness of Russian communities to accept vast changes of policy was established long before Marxian dialectic was thought of.

These two modes of adaptation to tension may be alternative cultural responses to a situation that every individual has to deal with in his own development. Mental growth results from a complex of contrasting impulses of love and hate, and our picture of ourselves and the social world in which we live is at first permeated with images of fantastically good and fantastically bad people. It is commonly reckoned an advance towards maturity when we can recognise the good-and-bad in ourselves as well as the good-and-bad in those around us: we achieve an accommodating, not over-demanding, attitude to ourselves and to others. In some societies this flexible and tolerant way of social life is transferred to the community, and to those who are its symbol and executive. The State is not divine, nor yet is it abhorrent.

In the individual's relation to the State there is again a contrast between the democratic and the totalitarian societies; for the former have evolved a sociopolitical device by which the people, without disloyalty or disruption, can express hostility to authority. In England and the United States interest in politics is split into two. One portion is reserved for the Crown (in America for the Constitution and the Supreme Court), and discontent, however active, does not disturb it: the other portion is focused on the Cabinet, which discontent can remove from office without upsetting the fundamental relation to the central authority. But totalitarian nations have no comparable device. HITLER made himself a god to his people, and had no cabinet worth attacking. The leading one-party State of the present time, Soviet Russia, has likewise exploited the notion of an omnipotent ruler, and provides hardly any means by which people can legitimately express discontent with the policy of their government on major issues. Instead, the hostility that the rulers might incur by their shortcomings is often diverted to some external agency—a custom that menaces international harmony, by producing uncontrollable suspiciousness and a paranoid attitude to neighbours.

Another and different factor which makes the present situation dangerous is that the acquisition of great military force excites latent ambition which would otherwise lie dormant. We cannot ignore the fact that the invention and virtual monopoly of atomic weapons puts a strain on American statesmanship, and that possession of these instruments places excessive power in the hands of a minority of citizens. A nation which is by tradition democratic is thus labouring under some temptation to behave like an ambitious oligarchy—a temptation to which in the past we ourselves have sometimes succumbed, but to which at the moment we are not exposed.

England today stands between two great Powers who do not understand each other, and who might each be irritated into supposing that war would bring advantage to the world. If in such risky circumstances we are to justify our reputation for political common sense we should perhaps pause before committing ourselves emotionally to either side; for in so doing we should lose any remaining chance of serving as mediators. Moreover, we might run a risk of denying a principle for which our ancestors fought and died, and towards which we strive in our slow growth as individuals. Nothing is harder to remember in a time of crisis, but at no time is it more necessary to recall that it takes all sorts to make a world.

Digitized by Google

Streptomycin in Infantile Enteritis

IT has been shown that streptomycin given by mouth is neither much absorbed from the gut nor inactivated by intestinal organisms, and that in practicable concentrations it is bacteriostatic against *Bact. coli* and *Proteus vulgaris*, though the anaerobic flora and fæcal streptococci are not appreciably affected by it. There therefore seemed reason to hope that this antibiotic would be useful in some intestinal infections as well as in the preparation of cases for large-bowel surgery.[1] In his summary report on the Medical Research Council trials of streptomycin in non-tuberculous infections, WILSON[2] noted that the results obtained in infantile diarrhœa so far have been variable: some centres have reported benefit from 2–4 g. spread over a week, but others are not satisfied that their results have been significant. He remarked that in further trials streptomycin is being given to alternate cases. This is obviously a sound method to adopt in any therapeutic trial, but its application to babies presents difficulties, not only on humanitarian grounds. A retrospective survey of admissions to hospital with the diagnosis of gastro-enteritis will quickly demonstrate that this symptom complex is easily confused with a wide range of other conditions which can only be excluded by the most rigorous clinical and bacteriological examinations. Added to this, there is the overwhelming difficulty in avoiding cross-infection of the baby who, having had its bowel sterilised with streptomycin, is in the same ward as another baby receiving controlled treatment. Where this problem has been recognised, only by setting up a special unit for the purpose, and by employing two separate staffs to treat the infants before and after sterilisation of the bowel, has cross-infection been completely overcome.

What the doctor will want to know is, first, does the evidence so far obtained justify the use of streptomycin by mouth in these cases; and secondly, should these babies be treated at home or in hospital? In this issue JAMES and KRAMER report on 30 cases of infantile diarrhœa treated with streptomycin by mouth; and ARMITAGE's independent statistical analysis leads to the conclusion that "the results indicate a real improvement in the treated groups." A brief scrutiny of the weight charts can scarcely fail to impress the clinician favourably. The treatment had the remarkable effect of checking vomiting immediately; otherwise, indeed, it would have been useless to continue with medication by mouth. This put an abrupt end to the loss of fluid, the exhaustion, and the tendency to alkalosis which accompany persistent vomiting. As a result, the treated children could leave hospital within a fortnight of starting treatment, so that the risk of cross-infection was much reduced. The Finns,[3] who gave streptomycin mainly by intramuscular injection, have had similar successes; but giving the drug by mouth is certainly simpler and kinder than injecting babies eight times a day.

Admission of these infants to hospital seems to be essential, because there are at least three types of case grouped under the same heading, even after all the other causes of symptomatic vomiting and diarrhœa have been excluded. The cases with *Proteus vulgaris* in the stools have responded uniformly well to this treatment, and those in which no ætiological agent has been found may give equally good results. On the other hand, there is a third group of cases in which no response can be obtained, and these may well turn out to be due to a virus. This last group of cases commonly have blood in the stools, and at necropsy they show a totally different picture from the customary findings, in that sanguineous discharges are present in the serous cavities, with engorgement and ulceration of the intestines. A further reason for hospital rather than home treatment is that a small amount of streptomycin (about 5%) is absorbed and when carried round by the blood-stream it may be sufficient to render pathogens elsewhere streptomycin-resistant. Not only may the organism of a coincident urinary infection be so affected, as JAMES and KRAMER mention, but the organisms in a latent or unrecognised mastoiditis may acquire similar undesirable properties. It is true that such incidental infections would probably respond to penicillin or sulphonamides, but even so it will be less worrying for all concerned if these complications arise in a baby already under observation and treatment in hospital.

1. Kane, L. W., Foley, G. E. *Proc. Soc. exp. Biol., N.Y.* 1947, 66, 201.
2. Wilson, C. *Lancet*, Sept. 18, p. 445.
3. Leisti, P. *Ann. med. intern. fenn.* 1947, 36, 575.

American Plan

LAST January President TRUMAN asked Mr. OSCAR R. EWING, Federal Security Administrator, to report, on the state of the nation's health, and on plans "to raise the national level of health during the next decade." After consulting a body of some 800 distinguished American citizens—professional and community leaders, organised into 14 advisory panels—Mr. EWING prepared his report,[1] which has now been published with a covering statement by the President. It is an important document. Written in clear and vigorous English, it presents in 186 pages a remarkable fund of information on American health conditions, and it will be widely discussed.

Mr. EWING refers to the great reductions in mortality and sickness that have already been achieved in the United States, but points to certain conditions showing that much remains to be done. For example, every year 325,000 persons die from conditions that could have been prevented, 4,300,000 man-years of work are lost through bad health, and the consequent loss to the national wealth is some $27,000 million. Careful inquiries have revealed a serious lack of medical, dental, and ancillary personnel, and of hospital and teaching facilities. The number of practising doctors (190,000) is only 80% of the number needed; at the present rate of recruitment the deficiency of doctors in 1960 will be 42,000. In some special branches of medical practice there are greater shortages; it is estimated that the nation needs at least three times the present numbers of psychiatrists and pædiatricians. The lack of enough doctors is felt particularly now that the effective demand for medical services has risen. The American national income, the report says, is now "at the highest level

1. The Nation's Health: a Report to the President. U.S. Government Printing Office, Washington, D.C. $1.

Digitized by Google

in history; more people have the funds to buy the medical services that they need."

The shortage of dentists is even more pronounced, and the rate of recruitment is not even keeping pace with the increase in population. In 1940 there was one dentist to every 1870 persons; by 1950, at the present recruiting-rate, there will be one to every 1900. Similar deficiencies are seen in the supply of nurses, teachers, and public-health and research workers; and the number of hospital beds is not more than half what the nation requires. Moreover, these services are very unevenly distributed: in New York State the number of persons per doctor is 500, per dentist 1300, per nurse 400; but in the State of Mississippi the corresponding figures are 1500, 5200, and 2400. And even in the areas where such services are most abundant, many people cannot afford to make proper use of them. This, Mr. EWING considers, is perhaps "the basic lack" of the American "entire health effort":

> "A scant 20% of our people are able to afford all the medical care they need. About half our families—those with incomes of $3000 or less—find it hard, if not impossible, to pay for even routine medical care. Another 30% of American families, with incomes between $3000 and $5000, would have to make great sacrifices or go into debt to meet the costs of a severe or chronic illness."

To supply the health needs of the United States, Mr. EWING puts forward a ten years' plan for expanding health services, both preventive and curative. This plan would increase the medical schools and other professional training institutions so that by 1960 the number of doctors, dentists, and workers in the ancillary professions would have risen by 40–50%, and it would in the same period increase hospital accommodation by at least 600,000 of the 900,000 beds needed. It would also enlarge the present Federal endowment of civilian medical research until it reached a total of $80–100 million—if enough qualified workers could be found. Hence it would involve a large increase in the expenditure of the Federal government, and of the State and local governments; by 1960 the Federal government would be spending some $2312 million annually on civilian health services—twice the present sum—while the expenditure of the State and local governments would be at the rate of $1795 million. Even these vast sums, however, would not include the cost of the national health insurance scheme Mr. EWING recommends for adoption.

A movement to introduce compulsory health insurance into the United States began shortly after the war of 1914–18, but made little progress. It received a fresh impetus from the publication, in 1932, of the report of the Committee on the Costs of Medical Care, and in recent years it has had the active support of President TRUMAN. Mr. EWING discusses the various objections brought against it, but says that he sees "no other way of bringing adequate medical services to fully half of the American people." He therefore recommends that the President urge Congress to enact as early as possible a national health insurance system on the lines of that formulated in the report. It would proceed by four stages: (1) Federal legislation to settle the basic policies and important details, and provide for a three years' "tooling-up" period, during which the administrative machinery would be set up and the necessary agreements reached; (2) the "tooling-up" period; (3) provision of services up to the maximum resources available; and (4) expansion of the system until "comprehensive services are available to everyone, everywhere in the country." The system would be administered by the State and local authorities with some Federal supervision, and if it were applied only to the persons coming within the scope of the present American old-age insurance system, it would cover about 85 million workers and their dependants, forming rather more than 60% of the total population. The costs would be borne by contributions from the insured persons and their employers, which, beginning at a nominal rate during the "tooling-up" period, would, when the benefits began to be provided, be raised to about 3% of the earnings of the insured persons, half being paid by their employers.

Mr. EWING recognises that the success of his plan would depend on his securing the coöperation of voluntary health workers. He contemplates that in every local area a community health council would be formed to study local requirements and to work for their fulfilment within the framework of the national plan. He concludes his report with these words:

> "A popular movement for health, planning for health, working together for health, is in the last analysis the only way in which we can raise the standards of health in our own communities and for the nation. . . . If the people will get together—professional workers and public representatives alike—in citizen health councils throughout the country, we will have the satisfaction of proving not only that health is everybody's business but that it is good business, essential business, and successful business."

Process to Provide more Insulin

THERE is a world-wide shortage of insulin just now, but not because there is too little animal pancreas to go round. The pancreas of nine or ten oxen must be processed to provide enough insulin to control the average diabetic for a year, and there are probably $1^1/_2$–2 million diabetics needing treatment with insulin; but enough cattle and hogs are raised in the world to provide for them. The carcases that supply our meagre meat ration would certainly yield enough pancreas to satisfy the insulin requirements of the diabetics in this country. The reason for the shortage is that only about half the slaughter-houses are equipped for freezing pancreas for insulin extraction. As soon after the death of the animal as possible the pancreas is removed, trimmed free from fat, and kept in a refrigerator at —20° to —30°C until the insulin can be extracted. During their journey from slaughter-house to factory the glands must still be kept frozen; otherwise considerable amounts of insulin will be lost from tryptic digestion. Details of a new process discovered in Germany which it is hoped will alleviate the shortage by simplifying the collection of pancreas from the slaughter-houses have lately been revealed by Dr. Brock Chisholm, director-general of W.H.O. The process, developed by Dr. F. Lindner of the Höchst works at Frankfurt-am-Main, enables animal pancreas to be preserved without low-temperature refrigeration. By a comparatively simple treatment the glands are chemically dehydrated and they can then be stored or transported for several days at room temperature without deterioration. This method is simple and safe and can be applied without special training or equipment by the slaughter-house staff.

Digitized by Google

Annotations

A HUNDRED AND TWENTY-FIVE

THE LANCET is now 125 years old. Introducing the first issue, dated Oct. 5, 1823, the founder, Thomas Wakley, wrote:

"It has long been a subject of surprise and regret, that in this extensive and intelligent community there has not hitherto existed a work that would convey to the Public, and to distant Practitioners as well as to Students in Medicine and Surgery, reports of the Metropolitan Hospital Lectures. Having for a considerable time past observed the great and increasing inquiries for such information, in a department of science so pre-eminently useful, we have been induced to offer to public notice a work calculated, as we conceive, to supply in the most ample manner, whatever is valuable in these important branches of knowledge; . . . In addition to Lectures, we purpose giving under the head, Medical and Surgical Intelligence, a correct description of all the important Cases that may occur, whether in England or on any part of the civilized Continent."

"The great advantages derivable from information of this description, will, we hope, be sufficiently obvious to every one in the least degree conversant with medical knowledge; any arguments, therefore, to prove these are unnecessary, and we content ourselves by merely showing in what directions their utility will be most active: To the Medical and Surgical Practitioners of this city, whose avocations prevent their personal attendance at the hospitals—To Country Practitioners, whose remoteness from the head quarters, as it were, of scientific knowledge, leaves them almost without the means of ascertaining its progress—To the numerous classes of Students, whether here or in distant universities—To Colonial Practitioners—And, finally, to every individual in these realms. Consequently, we shall exclude from our pages the semibarbarous phraseology of the Schools, and adopt as its substitute, plain English diction."

"In conclusion—we respectfully observe, that our Columns will not be restricted to Medical intelligence, but on the contrary we shall be indefatigable in our exertions to render THE LANCET a complete Chronicle of current Literature."

Other journals have since been established to supplement our efforts in some of these directions. Seven reigns and seven editorships have brought many changes of accent and idiom. Nevertheless, most of Wakley's purposes are still pursued. Though he designed THE LANCET largely for the congenial task of incising abscesses in the body politic, he strongly believed in information as a means of developing medicine, and he looked beyond the profession to the public, whose health was to be promoted by simple methods of prevention as well as by elaborate methods of cure. This dual interest in medicine and in its application was responsible for the structure of his journal, in which signed articles on the science and art were associated with miscellaneous news and statements of editorial opinion. Some hold that nowadays a medical journal should confine itself either to scientific communications or to news and opinion; yet Wakley's pattern survives in all the weeklies. It survives because it reflects the peculiar union, in medicine, of science and humanism, of knowledge and practice. It survives, into times when original scientific work is often highly technical, because the doctor is not merely a specialist, or merely a general practitioner, or merely a sociologist, seeking merely useful information, but is an educated person capable of deriving pleasure, profit, and often inspiration from work in other fields besides his own.

Long the property of the Wakley family, THE LANCET is still privately owned, an independent journal which is not the mouthpiece of any society, party, association, or group. For this reason its right to express opinions has sometimes been challenged by people who say "You have no constituency: whom do you represent?" Let it be clear, then, that we do not claim any of the authority that comes of meetings and referenda: we speak only for ourselves. But we enjoy the same right of expression as anybody else who can use a pen and find a printer. If in so doing we wield any influence it is by persuasion solely; and we think it a good feature of democratic life that independent opinions, as well as facts, should be continually presented as a stimulus to thought and discussion. Independence, however, does not necessarily imply isolation, and our obligation to accept full responsibility for whatever we print without an author's signature certainly does not mean that we can accept full credit for what is good. In forming and stating editorial opinions we have enjoyed through the years, and still enjoy, the aid of a great number of colleagues; and THE LANCET is largely their work. Like other journals it is maintained alike by those who contribute, by those who advise, and by those who read; and we gratefully acknowledge all these kinds of help.

For a century and a quarter we have held our weekly market of observations and ideas. Nowadays there are innumerable other markets, serving a great stream of commerce; and ours has become relatively small. But we are proud to find it increasingly used by the profession in distant countries as well as in the "extensive and intelligent community" in which Wakley, 125 years ago, bravely set up his first stalls and booths.

BETTER HEALTH AND STRICTER ETHICS

Prof. John Ryle is one of those who have transferred their energies "from work in the field of clinical and personal medicine to new ventures in the field of social medicine—from studies (in a more academic regard) in individual pathology to studies in social pathology." That this implies no sort of divorce from humanism is proved again by his book of lectures given last year in the United States and Canada.[1] He deals, among other things, with social pathology in the new age of medicine now opening, with the light thrown on the ætiology of disease by social studies, with teaching and research (especially at Oxford in the department he has had the task of establishing), and with the measurement of health. His last two lectures (Social Medicine and the Population Problem, and Medical Ethics and the New Humanism) are specially telling. He calculates roughly the possible saving of life in these islands if the stillbirth and infant-mortality rates could be uniformly reduced to the levels of the best areas, if the preventable diseases of childhood were really prevented, and if accidental deaths and injuries were diminished by safety measures in home, in factory, and on the roads; and he points out that a diminishing death-rate should carry with it an improved health-rate and a further decline in the number of people prevented from fulfilling their lives as parents. Whatever the opinion of experts about the dangers of an increasing world population, it is human, and even reasonable, to believe that our own race has useful work to do, and should strive at least to replace itself in successive generations; and that children healthily conceived should have the chance to live, and live healthily. He estimates that if the population of England and Wales was as well fed as that of Denmark, stillbirths would drop by 6000 yearly; that if all classes had the same infant-mortality rate as the Registrar-General's classes I and II, we should save a further 7000 lives; and that if diphtheria immunisation was universal some 2000 children yearly who now die would survive. Among potent life-saving measures he includes national food and housing policies, better working conditions, improved and coördinated medical services, social-security legislation, and a national education policy "in which education for health—physical, mental, and moral—should come to play a far more significant part." Nor is his eye focused on the British Isles: "Wherever the opportunity for health, especially *in utero* and in the two

1. Changing Disciplines. London: Oxford University Press. 1948. Pp. 122. 12s. 6d.

Digitized by Google

decades which follow birth, is unevenly distributed, we must consider that our responsibilities remain unfulfilled."

In his last chapter Professor Ryle touches on a practice that has troubled many conscientious doctors—that of the serious surgical operation undertaken on a wide range of patients before its value has been assessed by adequate physiological study and by thorough follow-up of early cases. Operations are devised, and then studied by trial and error, by men of limited experience as well as practised ones. He asks whether, for example, vagotomy and vasoligation have yet been justified either by animal or human experiment, and whether the partial and temporary successes and the complete failures have been judicially studied and reported, as a counterweight to the complete successes. He believes the answer to these questions, and others equally searching, is either "No," or "We do not know." Experiments, usually simple and safe, carried out on patients who are willing volunteers and understand the purpose of the investigation are, he thinks, entirely permissible, especially if they aim to decide whether a given line of treatment will improve a patient's condition; they are harder to justify if they are designed merely to advance theoretical knowledge and if the patient must be persuaded to agree to them. He might have added something about the type of investigation which carries a risk, whether to life or health: cystoscopy in the partially paralysed bladder is perhaps a fair example. Who knows what the risks are exactly? The patient does not even know that there are any, and is given no chance of deciding whether he wants to take them; the surgeon usually has an "impression" about the risks in general, and an "opinion" about the risks for this patient; he also has chemotherapy at the back of his mind as a saving measure if things go wrong. Yet the risks, even of temporary discomfort, should always be carefully weighed against the information which the method is expected to yield. Professor Ryle would like every research clinician contemplating an experiment to ask himself three questions; and these might well serve, too, for those undertaking routine examinations: "Would I accept that this experiment or investigation should be carried out in similar circumstances on a member of my own family? If so, would I accept that it should be carried out without his full coöperation and consent? In the presence of appreciable risk, do the possible results for science or medicine help to justify the risk?"

We may also ask, he suggests, that new operations entailing a danger to life or subsequent health should not be undertaken by men of limited experience before their value has been proved by others; and that methods of follow-up should be much stricter, wherever possible including a personal interview by a trained medical social worker.

PATIENTS' READING

THE International Federation of Library Associations has a hospital subcommittee which met during the recent conference of the federation in London. The discussions revealed differences in various countries in the attitude of the medical profession and the extent to which reading is held to have a therapeutic value. In Denmark the service, which is entirely staffed by professional librarians, takes little if any account of the condition of the patient. In Great Britain the general attitude of doctors, with some notable exceptions, is to leave the patient an entirely free choice, though in tuberculosis sanatoria and mental hospitals there is a definite movement to enlist reading as a contribution to treatment. In France there is a good deal of difference of opinion among medical men. In Belgium the service is admirably organised by the Belgian Red Cross under the direction of professional librarians, who are encouraged to take a course in social science. The Red Cross librarians read all the books before circulating them, and have a code to denote any risks which may attach to issuing them to particular types of patients. In some hospitals in the United States the conception of the therapeutic value of reading has reached the stage of prescribing books like medicine, and requiring a report from the librarian on the effect on the patient.

At the meetings it proved possible to obtain general agreement to a resolution that, while preserving the liberty of the individual patient, the librarian must appreciate the possible effect of the book upon him. Also approved were resolutions that public librarians should have special training for hospital work, that the voluntary workers who distribute the books should have some training, and that the attention of doctors and all concerned with hospitals be directed to the value of this work.

MECHANICAL ARTIFICIAL RESPIRATION

THE "iron lung," introduced by Drinker in the United States in 1929, and its modification the Both respirator which Lord Nuffield generously provided for British hospitals, are still saving lives which would otherwise inevitably be lost from respiratory failure. The uses found for the Both respirator have ranged from the treatment of overdosage with paraldehyde,[1] hitherto almost invariably fatal, to the prevention of post-operative atelectasis.[2] Persistent apnœa is no longer regarded as necessarily deadly in hospitals possessing a Both respirator. In other circumstances the first-aid teaching, whether in medical school, factory, or police force, is to apply manual artificial respiration by the method of Schäfer or Silvester, or by the even simpler and more efficient[3] rocking method of Eve, until the patient recovers or is transported to a hospital, which in England is never very far. In America, where Lord Nuffield's benefaction has not been emulated, and where distances are much greater, a Society for the Prevention of Asphyxial Death has for many years been stimulating interest in this subject. With their vigorous affection for up-to-date mechanical devices, the Americans have been attracted to automatic means of artificial respiration, and breathing machines have been widely distributed for use in the mine, by the canal bank, or even in the gas suicide's bedroom. Some have even been adapted to supply the airman with oxygen under intermittent positive pressure at high altitudes. There has therefore been a constant search for cheaper, lighter, and more compact apparatus which is yet sufficiently robust. Commercial competition has stimulated a variety of designs, all working on the principle of direct inflation of the lungs by oxygen under pressure. Controversy has raged for years over the relative merits of the different patterns. Motley and his colleagues[4] show that in practice all are fairly satisfactory, and that all will oxygenate the patient better than the traditional manual methods. The apparatus gradually builds up the pressure under the face mask during the inspiratory phase and allows it to fall rapidly to zero (i.e., atmospheric) at the start of expiration, so mimicking natural unimpeded respiration. Surprisingly the "suck-and-blow" machines, which inflate the chest during inspiration and also suck air from it in expiration, proved to have no advantages over the more usual patterns which only inflate. It appears that the "suck" is but poorly transmitted to the interior of the thorax.

The possibility that mechanical artificial respiration may have side-effects on the heart has hitherto been discussed largely on the basis of clinical impression. Now Motley and his co-workers have shown how very

1. Macintosh, R. R. *Brit. med. J.* 1939, i, 827.
2. Mushin, W. W., Faux, N. *Lancet*, 1944, ii, 685.
3. Macintosh, R. R., Mushin, W. W. *Brit. med. J.* 1946, i, 908.
4. Motley, H. L., Cournand, A., Werko, L., Dresdale, D. T., Himmelstein, A., Richards, D. W. jun. *J. Amer. med. Ass.* 1948, 137, 370.

Digitized by Google

dependent is the cardiac output on the variations in intrathoracic pressure during the respiratory cycle. Any deviation from the normal in this respect is followed by a parallel alteration in the heart's output, though not always in the same direction. Thus a raised pressure throughout the respiratory cycle produces a proportional fall in the cardiac output. Provided the mask pressure drops rapidly to atmospheric at the end of inspiration, and provided inspiration and expiration are of equal duration, no cardiac embarrassment need be feared when using mechanical substitutes for normal respiration.

The wide distribution of small mechanical respirators may give the layman a new and perhaps undesirable conception of the treatment of asphyxia. This danger has been emphasised repeatedly by Paluel Flagg and Yandell Henderson in America. A few years ago, Flagg wrote [5]:

> "If a child inhales a peanut or a pin, he is hustled off to the hospital and receives every advantage of the bronchoscopic clinic. Should he be so unfortunate as to inhale something larger, a marble or a chunk of meat, he is no longer in need of medical help. Everything will be solved if the suck and blow apparatus used last week in the stevedore down the street can be secured."

Henderson [6] called the suck-and-blow type of machine "a back-step towards the death of thousands." In this country, until it is certain that the expense of mechanical respirators would be justified in lives saved, we cannot do better than train our doctors and first-aiders to use the simpler methods of treating asphyxiated people.

FOR SMOOTHER RUNNING

STORIES of patients annoyed and frustrated by the way they are received at hospitals are too common to be ignored. The chilly welcome, the unguided search for the ward, the long hours of waiting in the outpatient department, and the obligation to repeat the same basic facts to every hospital officer who asks, are familiar vexations to the people who use, and now own, the hospitals. Such bad hospital manners are often the outcome of an archaic system of administration in a hospital which has outgrown its floor-space and is scarcely able to deal with the work it is equipped to do. Trouble is caused by out-of-date filing systems, puzzling methods of registration and record-keeping, lack of an appointments system, and other remediable defects. King Edward's Hospital Fund for London, in the hope of clearing the way for better customs, recently held a short course for administrative officers, to enable them to study the admission systems in a number of hospitals which have lately been reviewing the subject. The course was supervised by Mr. S. W. Barnes, house-governor of King's College Hospital, and he and the members of the course have now drawn up a report of their findings.[7]

Of 8 hospitals visited, 5 made appointments for new and old patients. The arrangements work well if they have the support of the doctors on the staff; but as this, unfortunately, is not always ungrudging, the task of arranging the appointments system must be placed in the charge of "an enthusiastic and tactful officer who will study their individual needs and gain their active coöperation." It is better, Mr. Barnes and his colleagues decided, to make the system compulsory, no outpatients being seen without an appointment unless they are referred from the casualty department as urgent cases. This helps to make patients and their family doctors appointment-minded. A patient who arrives without a doctor's letter, saying he feels ill, is seen by the casualty officer and, if his condition is urgent, is referred to a consultant. The writers of the report believe an appointments system, besides saving the patient time and trouble, simplifies the work of the hospital in several ways: it saves space, eases the work of the records staff, shows which clinics are overcrowded, and ensures a steady flow of patients to the ancillary departments. The list of patients due to attend can be used by the appointments office when checking misplaced notes, and makes the counting of outpatient attendances easier. The writers recommend that there should be one central appointments office to deal with the attendances at all clinics and departments. Events can then be made to dovetail, the patient polishing off his visits to various clinics on a single day, and special reports on his condition being completed in time for his next consultation.

The medical staff, wanting to reserve cases for teaching, sometimes insist that they cannot do this until they have read the doctors' letters. At King's College Hospital the appointments staff, who have been told what types of case to reserve, open all letters and make appointments accordingly. In the case of old patients, consultants mark the folders of the cases they need for teaching. The medical committee should be told when clinics are booked up a long way ahead, since it may be possible to arrange an extra clinic; and a margin of time is usually left, when appointments are made, so that urgent cases can be fitted in.

Some long-needed strictures on the appearance of outpatient departments should be appreciated by patients. To ask a sick person to sit for hours on a wooden bench in a cheerless flagged hall, watching the fat neck of the man in front, or listening to the wheezing of a neighbour or the fretful crying of a tired bored child, is as good a way of turning his uneasiness to anxiety, and his anxiety to downright fear, as could well be devised. The report urges some overdue reforms—light-painted walls, coloured comfortable chairs, odd tables, and plenty of papers and magazines—something more like a doctor's waiting-room and less like an approach to a morgue.

Again, "the patients' opinion of the hospital will be largely formed by the way they are treated at registration"; hence registration clerks need to be "tactful, kind and patient, with a pleasing personality." Some good detailed advice on the management of waiting-lists should also promote the comfort of patients. They should be given some idea of the time they will have to wait, warned to tell their own doctor if they get worse, and given a new forecast by letter "at least every three months." This last, somewhat ironic, proposal shows what a wounded snake our waiting-lists have become.

Every hospital, the writers consider, should have a medical records committee to define policy and keep the wayward doctors to it. A standard design of case-sheet is advocated within the hospital, but not between hospitals, since this would damp initiative and stultify progress. Hospitals must go on testing new methods. Details of cabinets, filing systems, and staffing of the records department need close study. In silent comment on human fallibility, the writers advise that the records office should be locked after hours, and that those seeking notes at such times should be made to sign for the key.

The *Times* reports that the World Health Organisation is arranging a conference of government representatives from war-devastated European countries. At the World Health Assembly Soviet Russia supported a large programme of supplies for these countries, and it was decided that Europe should have a temporary office "for the liquidation of war damage" in the field of health. The conference, which will meet at Geneva on Nov. 15, will consider the nature of the services required.

Dr. ROBERT CRUICKSHANK has been appointed to the chair of bacteriology at St. Mary's Hospital as from Jan. 1, 1949.

5. Flagg, P. J. *Science*, 1944, **99**, 469.
6. Henderson, Y. *Ibid*, 1943, **98**, 547.
7. Some Observations on Hospital Admissions and Records. London: Published for the King's Fund by Geo. Barber & Son. 1948 Pp. 28. 1*s*.

Digitized by Google

Special Articles

MEDICAL EDUCATION IN THE UKRAINE

W. P. FORREST
L.R.C.P.E., D.P.H.
FORMER CHIEF MEDICAL OFFICER, UNRRA UKRAINIAN MISSION; NOW SPECIAL ASSISTANT TO THE DIRECTOR-GENERAL, WORLD HEALTH ORGANISATION, GENEVA

IN Soviet Russia all medical students are trained with a view to occupying planned posts in a State health system. For example, since children constitute about a third of the population and their care is entirely "dispensarised," it is intended that a third of all doctors graduating should have some special knowledge of pædiatrics. A similar arrangement holds for the other branches of the medical profession, but the targets are not always reached.

The system of education and the curricula are standardised throughout the U.S.S.R. In each republic all medical education is subject to supervision by the local Ministry of the Care of Health, which supplies the funds and the personnel, and the Ministry of Higher Education, which manages the institutes. These ministries are subject to supervision by the All-Union Ministries in Moscow. All professional examinations are All-Union examinations, so a minimal standard is maintained throughout the country, and a diploma or other qualification obtained in one part of the country is valid in every other.

CATEGORIES OF MEDICAL WORKERS

Qualified medical practitioners have received their training in higher educational institutes and are classified as follows: medical practitioners with "broad" specialisation; medical specialists with "narrow" specialisation; medical research specialists; assistants (teaching or research); aspirants; candidates; docents; professors; doctors of medical sciences; corresponding academicians; academicians.

Medical Auxiliaries.—The higher institutes are responsible for the education of pharmacists, and the lower institutes for that of dentists (not stomatological specialists), feldshers and feldsheritsas, pharmacists' assistants, and medical nurses.

State sanitary inspectors are educated in the higher institutes.

ENTRANCE EXAMINATIONS

A candidate for entrance to a higher institute must have attended a ten-year school for pupils aged 7–17 and either hold the silver or gold medal of that school or pass the entrance examination of the institute he has chosen. The choice of profession and institute is free, and students are given every facility to meet the professors to have the curriculum and prospects explained. This is a routine procedure during the last years at the ten-year school. Special privileges are accorded to war veterans and children of Heroes of the Union.

All entrance examinations are held on or about the same date, and the students must surrender their birth certificates and school diplomas on entry to the examination; hence it is virtually impossible for them to sit several examinations in the hope of passing one of them.

A candidate for entrance to a lower institute must have attended a seven-year school and is usually required to pass an entrance examination. Lower institutes are roughly equivalent to the technical schools in industrial education.

FINANCIAL ARRANGEMENTS

The financial arrangements are the same in principle throughout the Union; only the payments vary. All students receive stipends which are sufficient to maintain them and pay the very low fees. Outstanding students receive extra stipends, and the best get Stalin or Kalinin prizes, which take the form of a large increment to the stipends. The stipends increase from year to year, but cease if the student twice fails to pass his examinations.

The payment of fees by the students is intended to inculcate a sense of responsibility and ability to manage their own budgets. Thus, the students receive stipends of 220–700 roubles a month. They have dining-rooms and dormitories, recreational and games facilities, and many other amenities, all of which are free, except for a daily charge of about 3·5 roubles for three meals a day.

Fees amount to 300–450 roubles a year, but seldom more than 60% of students pay the full fees, privileges being given to special groups.

THE MEDICAL CURRICULUM

At present the course lasts six years but it may be extended to seven in the near future.

First Year.—The subjects are Marxism-Leninism (a form of training in logic and philosophy), Latin, English, physics, biology, and parasitology; a start is made on anatomy, histology, physiology, embryology, analytical chemistry, and biochemistry.

Second Year.—Students continue with English, anatomy, histology, embryology, the chemistries, and physiology. At the end of this year is held the "half" State examination—an intermediate examination which weeds out the unsuitable students. The following subjects must all be passed at the same time, failure in one involving failure in all: (1) human anatomy, (2) histology and embryology, (3) physiology, and (4) biological chemistry. Permission to "sit" again may be obtained and students are often placed in other careers.

Third Year.—Here the "broad specialisation" begins to influence the subjects taught. The students start the study of microbiology (bacteriology), pathological physiology, pharmacology, pathological anatomy, diagnostics and "private" pathology and therapy, and general surgery. He has commenced clinical attendances in his second year (some even start in the first) and will continue these until the end of the course. At the end of this term there is an examination (not a "State" examination) and the student does his first "physician's practicum." He repeats this in the summer of the fourth year and in the fifth summer will do his "physician's subordinator"—a form of internship. These clinical periods involve about seven hours a day for at least three months.

In the *fourth year* the students really begin their specia training as general practitioners, pædiatricians, sanitary physicians, &c. There is an examination at the end of this year.

The *fifth year* sees the completion of the apprenticeship and many of the smaller subjects, such as venereal diseases, pædiatrics, tuberculosis, infectious diseases, ophthalmology, radiology, &c. The range of these is complete; there are no omissions.

The *sixth year* is more intensely clinical, finishes off the special subjects, and completes the intensive clinical studies.

The number of hours given to each subject is shown in the accompanying table.

FINAL STATE EXAMINATION

The final examination (known as the "full" State examination) always has nine subjects, every one of which must be passed at the same sitting.

A. *General Medical Faculty* ("*broad specialisation*")

1. Human anatomy
2. Pathological anatomy
3. Pathological physiology
4. Internal diseases (=medicine)
5. Surgical diseases
6. Obstetrics and gynæcology
7. Infectious diseases
8. Children's diseases
9. Hygiene

Digitized by Google

B. *Pædiatric Faculty* ("*broad specialisation*")

1 to 6 as above
7. Children's diseases
8. Children's infectious diseases
9. Hygiene

C. *Faculty of Sanitary Physicians* ("*broad specialisation*")

1. Microbiology
2 to 5 as above
6. Epidemiology and infectious diseases
7. Environmental hygiene
8. Hygiene of "feeding"
9. Hygiene of labour (industrial medicine)

The successful student is entitled to a diploma which states that he has passed the State examination, that he has studied six years at the institute, and that he is a qualified physician with broad specialisation in whichever subject has been his specialty.

Examinations (except State examinations) are not so important as the personal file, which is kept for each student and shows every detail of his academic career. This is on the examiner's table. It is also used at the State examinations, where it usually has no more than 50% significance.

Some of the smaller institutes only graduate students of group A.

ON GRADUATION

A newly qualified doctor commands a salary of 800 roubles or more a month according to his record. Housing is guaranteed—a tremendous concession—and is free. Special rations of food and clothing are granted, and in the country the doctor receives a garden, a cow and other livestock, and special rations of fuel and other scarce commodities.

An inspector from the All-Union Ministry of the Care of Health meets the graduates and shows them the list of vacancies, from which they choose. The best students are retained by the professors for training as research-workers and teachers. The professor who has vouched for such a student must report every six months to the Uchonny Soviet—a council of research-workers. This enables a control to be kept on all such workers.

Except those taken for research or teaching, all graduates must spend their first three years where the ministry wishes to send them—i.e., they are subject to direction. Many stay on in the posts to which they were directed, after the end of the three-year period.

RESEARCH

The division of institutes into teaching and research entities, so extensively practised in all other branches of science in the U.S.S.R., has been fought by the medical profession. They have retained the more familiar mixed institutes, and are quite elated about it, since some other professions are now convinced that the medical profession was right. So these teaching institutes are 50% research, and the teaching staff divides its time equally between research and teaching. Research in this country very often involves large hospitals and much clinical work.

MEDICAL AUXILIARIES

Pharmacists and State sanitary inspectors are trained in higher institutes, and all the other medical auxiliaries in lower institutes.

Pharmacists are employees of the Ministry of the Care of Health and operate chemists shops controlled by that ministry. Supplies come from the Ministry of Medical Industry. They have a four-year course and receive diplomas.

State sanitary inspectors are in a rather different category, since the State sanitary inspection is an independent organ of the central government, responsible to the local health authorities at each level, but with power of appeal to the chief of the State sanitary inspection in the Ministry of the Care of Health in Moscow. Thus he has direct access to the Council of Ministers of the U.S.S.R. It is therefore both an operative and a controlling organisation. It possesses the widest powers, and woe betide the wretched plant manager or even State minister of health who contravenes the sanitary laws. In practice, little friction arises, and a most useful function is undoubtedly performed by this service.

State sanitary inspectors who are always medically qualified, have a 1–2 years' course in special institutes of sanitary science and receive a diploma. The curriculum in these courses covers all the usual aspects of sanitary science including industrial, food, meat, and environmental hygiene, and the hygiene of public utilities. The course and the policies are decided according to the latest medical hygienic opinion supplied by the All-Union Ministry of Health. One of the deputy ministers of health of any republic or State is always a sanitary inspector.

The other medical auxiliaries are all educated in lower institutes and spend some time as apprentices to experi-

ALLOCATION OF TIME TO THE VARIOUS SUBJECTS OF THE CURRICULUM

Subject	Medical faculty		Pædiatric faculty		Hygiene faculty	
	Years of course	Total hours	Years of course	Total hours	Years of course	Total hours
Marxism-Leninism	1 & 2	250	1 & 2	250	1 & 2	250
Latin	1	108	1	108	1	108
Foreign languages (English)	1 & 2	190	1 & 2	190	1 & 2	190
Physics	1	144	1	144	1	144
Biology and parasitology	1 & 2	216	1 & 2	216	1 & 2	216
Human anatomy	1 & 2	398	1 & 2	398	1 & 2	398
Histology and embryology	1 & 2	250	1 & 2	250	1 & 2	250
Inorganic and analytical chemistry	1	162	1	162	1	162
Biochemistry, including physical and colloidal chemistry	1 & 2	374	1 & 2	374	1 & 2	374
Physiology	2	278	2	278	2	278
Microbiology	3	255	3	255	3	255
Pathological physiology	3	162	3	162	3	162
Pharmacology	3	219	3	219	3	219
Pathological anatomy	3 & 6	264	3 & 6	264	3	228
Diagnostics, "private" pathology and "private" therapy	3 & 4	332	3 & 4	332	3 & 4	332
General surgery	3 & 4	213	3 & 4	179	3 & 4	196
Operative surgery and surgical anatomy	4	127	4	113	4	119
Hygiene	4	254	4	260	4	119
History of medicine	4	34	4	34	4	34
"Faculty" therapy including a course on tuberculosis	4 & 5	276	4 & 5	208	4 & 5	214
"Faculty" surgery	4 & 5	248	4 & 5	180	4 & 5	180
Dermatology and venereology	4 & 5	124	4 & 5	124	4 & 5	107
Nervous diseases	5	138	5	124	5	110
Organisation of the care of health	5	85	5	96	5	96
Midwifery and gynæcology	4 & 5	279	4 & 5	192	4	192
Practical obstetrics	...	q.s.	...	q.s.	...	q.s.
"Hospital" therapy (medicine)	5 & 6	304	5 & 6	184	5 & 6	198
"Hospital" surgery (including short course of jaw surgery)	5 & 6	332	5 & 6	240	5 & 6	184
Diseases of children	5 & 6	212	...	...	6	70
Infectious diseases and epidemiology	5 & 6	184	5	124	5 & 6	132
Diseases of the eye	5 & 6	96	5 & 6	82	6	72
Diseases of ear, throat, and nose	5 & 6	96	5 & 6	96	6	72
Psychiatry	5 & 6	100	6	92	6	70
Forensic medicine	5 & 6	100	6	84	6	84
General course on children's diseases	..	..	4	124	..	..
"Faculty" pædiatrics	..	..	5	158	..	..
Hospital pædiatrics and tuberculosis in children	..	..	6	248	..	..
Infectious diseases of children	..	..	5 & 6	128	6	96
Special surgery of children	..	..	6	128	..	..
School hygiene	..	..	See Hygiene			
Environmental hygiene	..	..	..	..	4 & 5	228
Hygiene of food	..	..	..	..	4 & 5	169
Epidemiology	..	..	..	..	5 & 6	166
Industrial hygiene	..	..	..	..	5 & 6	230
School hygiene	..	..	..	..	5 & 6	92

Digitized by Google

enced members of the same profession before taking up independent work. It is planned to have four medical auxiliaries for every one doctor.

Dentists are really dentists' assistants and always work under the supervision of stomatological specialists, who are medical practitioners whose specialty is the mouth. They have a three-year course similar to the old four-year dental courses in other countries but with more emphasis on the practical side and less on academic work. They work in stomatological clinics, children's clinics, mothers' clinics, factory polyclinics, and in rural areas.

Feldshers and Feldsheritsas.—These are mostly to be found in rural areas or where there is a population too small to support a full-time doctor—i.e., less than 1500 population. The Feldshers provide the lieutenants and sublieutenants of the army medical service, and usually do much the same work as would be done by highly qualified nurses in the U.S.A. and U.K. They operate feldshers' points in the country, usually one for each small group of villages or collective farms, and small sanitary points in factories too small to have a factory doctor or polyclinic. Their duties are strictly laid down, and they are always responsible to the district medical officer, who they must call in or consult for any occurrence above a given level and in all cases of infectious disease. They do the doctor's "donkey-work" in the country and provide first-aid. They are educated in lower institutes for three years. The training is again more practical than academic but is very well designed for the duties they have to perform. They receive a diploma and serve their first two years as assistants to experienced feldshers in the field, after which they manage their own point or practice. They have a most important educational function and are the first link in the collection of rural statistics. Feldsheritsas are permitted to work in towns to be near their husbands. Over 60% of all feldshers are women.

Feldsher midwives receive a three-year course (almost exactly the same as the course for midwives in Scotland but more extended, with greater practice) in lower institutes. The feldsher midwife serves in maternity homes and hospitals in the urban areas and is in charge of the lying-in houses which must be provided by the collective farms. She manages these, looks after antenatal and postnatal care, arranges consultations, and registers all pregnancies and births. Her duties are strictly laid down, and she is responsible to the local doctor for maternal care. She carries out much educational work.

Medical Nurses.—It is to be expected, in view of the existence of feldshers and feldsher midwives, that nurses would come in rather lower down the medical scale, and such is the usual case. Nurses receive two years' training in lower institutes, including much practical work (half of the time) in hospitals and polyclinics, and receive a diploma. They are not commonly seen in the countryside, except in village hospitals, polyclinics, or ambulatories attached to the district medical headquarters. Their sphere of action is in the urban areas, where they are to be found in all medical institutions. Extensive facilities are provided for them to improve their status, especially in the field of the care of children's health, where they can become directors of orphanages, nurseries, and other institutions maintained by the health authorities for children up to the age of four. They are also to be seen in sanatoria and rest-cure establishments. All discipline of nurses is always the responsibility of the chief nurse of the institution who in turn is responsible to the director; she does not have the other administrative functions of the U.S.A. or U.K. matron. It is unusual for a nurse to be responsible to a feldscher.

Pharmacists' assistants stand to the pharmacist as dentists do to the stomatologist. They are trained for 2 or 3 years and serve in chemists' shops.

POSTGRADUATE EDUCATION

Postgraduate education has been instituted by law "continually to raise the qualifications of medical workers of all kinds." Facilities are available for all medical workers to take refresher courses arranged, in consultation with the requisite institute, by Oblasdrav (roughly equivalent to county medical administration). The worker is notified and goes for various periods of a month upwards to the institute to which he is directed. While he attends the institute he receives a stipend almost equal to his salary, and his family receives his salary. No fees are charged.

In the Ukraine there are four institutes for postgraduate studies for physicians: Kiev (the oldest), Kharkov, Odessa, and Lvov (the newest). The postgraduate work is usually, but not always, combined with specialisation to fit the practitioner for a more important post in Oblasdravotdel (county health-administration affairs).

Apart from raising the standard of proficiency of the medical practitioners and bringing their knowledge up to date, and providing further specialisation (but not making them specialists) these institutes provide one of the main channels for training medical specialists for teaching and research. This is done by providing "ordinature"—i.e., internship and training for medical specialists—and "doctoranture"—i.e., facilities for preparing an M.D. thesis. The institutes do not give degrees as doctors (or candidates); these are given only by the Academy of Sciences, which works in close coöperation with the institutes. This work usually takes 2 or 3 years. The institutes also coöperate in research work, which is always closely integrated with teaching. The various faculties of the institutes are usually in the same premises as the research units.

Registers are kept of all doctors who have passed through the institutes, and these records are available to assist any other health institution in staffing problems. The institutes advise Oblasdrav on optimum staff requirements, as regards both numbers and specialisation, and encourage Oblasdrav in raising the general standard of its employees. This is a two-way arrangement and in no case constitutes direction of one party by the other. Oblasdrav is obliged to listen to the advice of the institutes, and vice versa.

These institutes are large and are not located in one building, and several chairs are attached to each large teaching and research hospital or institute. In Kiev there are thirty-three chairs, which can prepare students for more than 33 specialties. Thus the entire range of postgraduate medical study is fully covered.

THE FINISHED PRODUCT

It is difficult for a stranger to assess the finished product, but by all pragmatic standards the graduates appear to be as well qualified as their contemporaries in other countries, and indeed better than in some. To judge by the curriculum and the calibre of the instruction, they must be better prepared than most, but the present serious shortage of specialised equipment undoubtedly nullifies some of the advantages of the very full course of instruction and practice. This will pass, however.

To judge by results, the students are very well trained indeed. Medical teachers declare that the graduate of today is vastly superior to his predecessor of even ten years ago; they proved themselves well able to do excellent work in the appalling conditions and almost total lack of modern facilities prevailing during the occupation; it is generally recognised that they did excellent work with the Red Army; and there have been no epidemics in Russia, in spite of ideal circumstances for outbreaks of infectious disease.

It is considered that other countries have something to learn from the educational methods in force here, and

Digitized by Google

especially from the integration of medical education with the national requirements for medical personnel.

I am indebted to the Hon. I. F. Kononenko, formerly Minister of Care of Health for the Ukrainian S.S.R., and Dr. Lev. I. Medved, now Minister, who have accorded me every facility; Prof. S. S. Kagan, chair of organisation of health, who has been my guide, philosopher, and friend; Professor Kalchenko, director of the Kiev Postgraduate Institute; Docent Kalainichenko, director of the Kiev Medical Institute, and all the other professors, docents, and physicians who have supplied me with information.

MEDICAL PROTECTION SOCIETY

Sir Ernest Rock Carling, the president, addressing the annual general meeting of this society held in London on Sept. 29, said that it had had another successful year: the membership had steadily increased and the financial position was sound. With the coming of the National Health Service the future was uncertain; but nothing in past experience suggested that attacks on the profession by disgruntled patients would grow fewer. Government departments had a tendency to compromise, without clearing the character of the professional person attacked; and lawyers were inclined to exaggerate the alleged shortcomings of the medical man, attributing to his neglectfulness and hard-heartedness—if not actual malice—the entire effects of accident or disease. The costs of medical protection were likely to rise rather than fall; but the society faced the future with confidence and solid assets. One advantage it might gain from the National Health Service was that the doctor would have to keep good records; for in the past many a case had been prejudiced for lack of notes.

Remarking on the trouble caused by broken hollow needles, Sir Ernest said that in all cases where the society had submitted the fragments to a metallurgist a manufacturing defect had been found. He hoped for improvement of manufacture, but also reminded members that needles must not be cleaned with, or immersed in, solutions of iodine, which even in minute traces could erode and weaken them. Another source of frequent trouble lately had been fracture of the jaw during dental extractions. This was by no means always the result of bad work: it was often due to osteomyelitis, which could be properly treated only by removal of the offending teeth. Nevertheless wherever there was a possibility of osteomyelitis leading to fracture it was important to radiograph the jaw first.

Where there was some mishap the doctor or dentist was often uncertain whether he should tell the patient (or the relatives). In the vast majority of cases the patient should be informed: to give the facts never redounded to the practitioner's discredit.

The objects of the society, said Sir Ernest in conclusion, were not merely to protect medical men: having the same objects as medicine as a whole, it was concerned with prevention as well as defence, and it sought at all times to encourage correct professional behaviour.

The society's expenditure for the year 1947 averaged 23*s.* 3*d.* per member, though the subscription remained at £1. With accumulated funds standing on Dec. 31 at £112,991, the resources available for protection were £145,816, and the society is reinsured to an unlimited amount against adverse costs and damages exceeding a specified amount during any one year.

Tribute was paid at the meeting to the late Mr. G. F. Stebbing, who has been succeeded as chairman of council by Dr. G. M. Stoker. Sir Robert Hutchison spoke in warm terms of the service rendered to the society by Sir Ernest Rock Carling, who was re-elected president.

Mr. W. M. Mollison will serve again as treasurer.

Dr. A. R. French was appointed secretary of the society in place of Dr. R. W. Durand, who is going to Belfast as medical superintendent of the City Hospital.

Disabilities

14. POLIOMYELITIS

I CONTRACTED poliomyelitis two years after I had qualified. During the first epidemic in Dublin, in April, 1941, I developed what seemed to be a full-blown meningitis. Lumbar puncture was a great comfort. Paralysis developed over two days, from the legs upwards. At its height I could just breathe unaided by concentrating hard, and chewing, swallowing, and facial expression were unaffected; otherwise I could only move my fingers and turn my head on the pillow. For three days I had retention of urine and double vision. In the next week there was a decided improvement, and thereafter a very slow recovery. I developed extreme tenderness along the nerves and tachycardia, both of which persisted for 6 months. After 4 weeks' illness, for reasons of occupation and economy, I asked to be brought home, though I was sorry to leave the fever hospital, where everyone was wonderfully kind to me.

Being impatient for recovery, and encouraged by the delusion that I would soon reach it, I worked hard at my muscles from the start, despite the invariable appeal of those days to "avoid overdoing it." By the 6th week I could turn over in bed in 45 minutes, by exerting systematic traction on my pyjamas and sheets and levering my pelvis sideways with my knuckles. By the 3rd month I could travel slowly round the bed. It still took me five minutes to turn over, and I felt faint in ten minutes if I sat up, despite a firm abdominal belt. I was so wasted that my finger and thumb would meet round my arm from wrist to elbow and from elbow to shoulder. At 6 months I could just manœuvre myself off my low bed on to my hands and knees on the floor and back again, and at 9 months I could struggle up sideways into a sitting posture, crawl short distances, and negotiate a flight of shallow steps with the combined technique of worm and monkey. I still felt faint after half an hour's sitting. At 10 months I was promoted to a wheel-chair, and at 1 year I could get in and out of it unaided; what's more, when placed on a tricycle I could drive it eighty yards round the garden, with the help of a hoe.

At 1½ years I was travelling round the house and up the stairs on my feet, clinging to furniture or banisters, and I could walk round the garden clinging to a rope. I did two miles on the tricycle every two or three days, and in the next 6 months I increased my rides to eight miles. I was beginning to walk alone, bent over two sticks, and was learning to bicycle in a narrow corridor, where there is less scope for falling. Most of my time was still spent lying down. At 2½ years I was walking upright, with one stick, for two miles or so and doing some digging and fuel stacking. I had discarded my abdominal belt. By 3 years I could do extensive heavy work, ride 40 miles on my bicycle, and pull myself up to my chin on a horizontal bar twice. I still lay down for half the day. At 3½ years I could walk ten miles without a stick in five hours and could just get up from a flat surface, if it was not too smooth, without a stick.

It is now 6½ years since my illness. Progress has been slower in the last 2 years or so, from flagging enthusiasm and greater demands on my time. I can sit without slouching, stand erect, and keep my hips steady when I walk, so my gait attracts no notice. My maximum speed on foot is five miles in 1¾ hours. Stairs are still awkward, because I cannot yet stand on one leg with a bent knee.

* * *

From my own experience and other people's, the general idea that early return of voluntary muscle power is a good sign seems to be justified, for muscles that improve well at first maintain their lead and can be expected to become powerful if exercised. On the other hand, state-

Digitized by Google

ments like the following from a well-known textbook are misleading: "Muscles that are going to recover useful power will already have done so by the third month." All my muscles recovered more strength in the second 3 months than in the first 3, and much more in the second 6 months than in the first 6. Almost all my muscles developed considerably more in the second year than in the first, and most developed more in the second 2 years than in the first 2. My weaker muscles are still improving, with increasing returns for any effort I put into them. My interest has returned, and dancing is the next target. A friend of mine is improving after 18 years, during 9 of which there was complete neglect. There seems to be no time limit to improvement of strength. The slowest progress in rehabilitation, apart from the spontaneous recovery after the acute phase, is actually at the beginning.

The arch enemy of the poliomyelitis patient is stagnation, from the first day of his illness until he is sound again. Physically, mentally, and morally he must be kept fresh and stimulated by every means in the doctor's power. In the acute stage, frequent passive movements are a great delight. One never loses the wish to move, and the craving is strong in the early days. Frequent friction and gentle massage all over are highly refreshing, and warmth will prevent the cramps which come on when the limbs are raised. With plenty of gentle handling the tenderness disappears more quickly than without, and incidentally, it disappears quicker in the more exercised muscles than in the others. Deep abdominal massage, particularly in the acute stage and the first few weeks, helps to stave off the petty miseries of constipation and purges and enemas, flatulence and indigestion. As soon as the temperature drops every muscle should be exercised to halt atrophy from disuse. Electricity is good at this stage if the patient can stand it.

After the first month or so one's morale tends to weaken. Progress can be so slow that patients sometimes regret their escape from death. Initiative may well collapse altogether, with spasmodic revivals. Everything is worse when one begins to get out and about. People are kind to the physically hampered, and there can be a certain humour in an old lady or an errand boy pushing one's tricycle up an incline or over a bridge. But nothing will prevent humiliation when one has to spend hours, with frequent rests and the next day flat in bed, travelling a distance an ordinary person covers in a few minutes.

The doctor who is an understanding friend can work wonders—if he has the time and the necessary knowledge of mechanics. A special institution is a perfect environment; here the patient will learn a lot from his fellows, even if he is a child, and he will be instructed on questions of apparatus. Failing that, the patient and his family must be organised at home, but it is hard for the poliomyelitis victim on his own to exercise himself as he should. He rarely if ever does. Some muscles are likely to be forgotten, as often happened with my back and abdomen. Careful and complete records, regularly filled in, will reveal many little improvements that would otherwise pass unnoticed.

A purposive mental or manual occupation is essential, preferably with some responsibility, or under the orders of outsiders, and if possible remunerated. It may be necessary at times for the doctor to tell a patient who is on his own to stop being sorry for himself and think about something useful. He should be encouraged to be independent and look after himself, even if he finds this difficult. Poliomyelitis cripples in the same neighbourhood might derive much mutual encouragement if they kept in touch with each other, making a sort of club.

If there are many weak muscles both doctor and patient may need to do much reading and discussing to win real progress. Fatigue is an essential part of the development of a muscle. Nature seems to provide a reserve beyond ordinary demands, and if this reserve is steadily encroached upon she builds up a larger one. It is the activity that the patient can only just perform, or cannot quite perform, that will bring back his strength. If increasing demands are not made, one can expect no improvement. Surely this applies to any training, physical or mental? At the end of a session of effort the muscles should be appreciably weaker.

Pain in a muscle as the direct result of exercise will follow a sudden large increase of effort, and will not return when that new effort is repeated. It appears to be without harmful significance; when my muscles became sore they gained strength faster than at other times.

There is a difference between developing strength and developing stamina, but both are important. Plenty of routine physical activity, carefully graded, will build up stamina. Special short sessions designed to produce rapid fatigue will increase strength. As the patient recovers the short sessions should be increased in number, and he should be encouraged to move more rapidly. The American idea of putting weights on the patient—lead insoles, for instance, or a bag of shot round the ankle or wrist or elbow—is excellent. Progress is a matter of compound interest; a stronger muscle gains strength more rapidly than a weak one. The dreary work of the first few months may seem entirely futile, but it is indispensable.

Fatigue can be dangerous if it is cumulative, and there is some justification for the usual concern. Muscles can shrink and the patient become a nervous wreck. There must always be sufficient rest to correspond to the exercise. If the routine is so planned that the muscles recover their best strength at some time every day, or even every two or three days, there is nothing to fear. When he is not taking exercise the patient should spend most or all of his time flat in bed. Meals can be taken quite conveniently from a tray on the chest; the head should be as vertical as possible, with the shoulders flat on the bed. This posture is much more comfortable than it looks, brings no deformity, and was my favourite one for over three years. The extra energy saved is surprising.

If the diet is poor, progress will slow down, for there is something peculiarly depressing about trying to exert oneself on poor food. A full diet, with sufficient minerals and vitamins, makes an obvious difference; and extra iron and vitamin C now and then are a help.

The most convenient apparatus for home use is an overhead hook or beam, at a good height. To this spiral springs (much handier than weights and pulleys) can be attached, or plain cords. Limbs mounted in slings can make any movements needed, without the influence of gravity, if the patient is in a suitable position. Gravity can be gradually brought into play by lowering the fixed point and shortening the cords. If the shoulder muscles are recovering, a back brace is a hindrance rather than a help. Very little attention will prevent scoliosis or other deformity. Good gutter splints are comfortable for *resting* the legs in, but there should be no flexion at the knee, however slight.

I found a 'Dunlopillo' square more comfortable and reliable than an air ring. But, when one's back muscles are negligible, deformity will result if the pelvis is kept raised, so I used a flat pad of sponge rubber, covered in soft cloth, with a hole just large enough to accommodate the prominent part of the sacrum.

* * *

To sum up: There is no apparent limit to progress. The beginning is the slowest. A special institution is desirable. Fatigue is absolutely necessary for muscle development, but rest and proper diet are also essential. Loss of morale and general stagnation can be the patient's biggest trouble.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

AFTER reading the correspondence in THE LANCET I have been asking myself just what constitutes a good secretary for a consultant. First, she must be able to take notes at a high speed. For this she will require acute and accent-filter hearing, flexible fingers, courage (the girl who blenches at the thought of confining the shorthand outline for "dysdiadochokinesia" to one line of her notebook won't last long), and a better fountain-pen than has yet been invented. Still more important, she should be able to read her shorthand. She should be able to spell medical terms not only correctly but with that brand of correctness most acceptable to her employer—e.g., clinique, clinic; leukocytosis, leucocytosis—and her typewriting should be accurate. In medical typescript trifling errors and omissions assume alarming proportions and can be misleading in a manner likely to lower the dignity of the writer: "No puss was found in the urine but some cats were present." A knowledge of Latin is helpful, but the scholarly secretary should never seek to minimise her shortcomings by murmuring in the chief's ear, "*Humanum est errare*"; he would agree that to err is, but not that secretaries are.

It is not desirable that a secretary should have a sense of humour. If, for instance, in a moment of illumination she suddenly sees the heart specialist's reiterated advice to his patient to "learn to take things quietly" as lesson 1 of a correspondence course in burglary, she will be so busy visualising the students, plus masks and dark lanterns and minus boots, striving to take things quietly that she will get the dosage of digitalis wrong; and, unless her chief reads his letters as well as signing them, will probably end on the gallows. She should, however, have enough imagination to tell her what the doctor meant to say when his dictation is more than usually elliptical, but not enough to enable her to identify all the symptoms of all the patients with the sensations experienced and the activities engaged in by her own body.

She must be clairvoyant. How else will she bring to the chief's notice engagements he has omitted to tell her he has undertaken? How else will she "remember" to get the results of an X-ray examination that she didn't know had been done? Above all, how else will she know to refrain from rendering accounts for fees that were paid to him at the time of consultation and never spoken of again? It is useful and sometimes essential to be able to read the chief's writing; but that is asking rather a lot, and I have found that surgeons may even like to be appealed to for an interpretation. They get some sort of psychological kick out of feeling that they have stumped one—something akin, I suppose, to having planned the perfect crime. Freud would know.

Consultants sometimes want their secretaries to attend them at hospital, and that brings up a whole series of new difficulties, the most outstanding being the sisters. To cope with these calls for tact, technique, and tolerance; the secretary who can convey the chief's instructions to his ward sister without producing an immediate reaction of resentment to herself as intermediary, antagonism to the idea contained in the request, and obstructiveness to its being carried out, has got what it takes. If she can, in addition, extract from one of the secret sisterhood the information she requires without effusion of blood and tears, that secretary is worth her weight in coal.

* * *

Being employed as a corporation medical labourer, and well conditioned to "such other duties as from time to time, &c.," I had no choice but to accept gracefully the unsought honour of medical examiner to the local police, without of course any addition to what is called my salary. The candidates all proved to be fine handsome fellows, and their presence in the clinic has made life more interesting for the female clerk, who finds them more exciting than the usual crowd of workmen's compensation crocks and in the main superior to those whom the nurse will call "superannuees." On the medical side they proved to be less interesting. Every man had an unblemished medical history, and clinical examination has so far failed to detect any of the many abnormalities listed in the 6-page booklet which has to be duly (why "duly"?) completed. The swelling totals of "Normal's" and "No's" made me wonder if I was losing my touch. However, the other day an elderly member of the force came along for examination with a view to retiring on pension. He had plenty wrong with him, and fruitful results were obtained in almost every system. His past record of illnesses filled a typewritten sheet, which showed ample evidence of illegible writing on the part of his doctor and praiseworthy attempts to decipher it on the part of the typist. "Turunculosis" of course was furunculosis, and "Unpitijo" was resolved into impetigo, but "Phonjijitis"!—what an admirable term for the jumpiness which betrays a doctor in non-medical company when the telephone rings! The best we could think of was pharyngitis, but as the would-be "retiree" swore he never had a sore throat the matter rests here.

* * *

It may not be good for us peripatetic correspondents that, secure in our anonymity, we can ventilate our opinions without contradiction, or expurgate our pet grievances without denunciation—but it is very pleasant. I wonder sometimes how far our identity is suspected. Notwithstanding all precautions, the choice of subject or some eccentricity of style often betrays a writer. But though they may suspect, our victims cannot be sure. So we may mingle with colleagues whose quiddities we have limned, and sympathise hypocritically with their grumbles while inwardly preserving the opinions we have recorded.

As I expected, my criticism of eminent lecturers excited some protests. I am impenitent. A formal lecture, such as those delivered at the colleges, should be not the mere reading of a manuscript, but a thoroughly prepared oration delivered with the aid of a few notes or even none at all. To the silly objection that the Address has been learnt by heart, I would reply that this is following the practice of all great orators including Cicero, and is in any case no small achievement. Admittedly the preparation demands a great deal of trouble, and the performance a great deal of courage. The fear of a complete blackout can never be entirely absent even in the experienced accomplished performer; yet discipline demands that the lecturer should be confident enough to refrain from carrying a manuscript in his pocket—just in case. The perfect exponent is he who is so expert in his subject and so saturated with it that his uninterrupted fluency gives the impression of impromptu delivery. For this not a little of the histrionic is essential.

Is it worth while? That must be a matter of opinion. I know at least three members of our profession who have demonstrated their ability to perform such a tour-de-force, and if they acquire a sense of satisfaction commensurate with the admiration of their audiences they are well rewarded for their trouble.

* * *

As I am unable to accept the following offer, I pass it on for the use of some more artistic and discerning reader.

DEAR SIRS,—I am taking the liberty of writing to you now, about if you can sell your body for a small fee to your own university, for medical research work, at my death, can that be so, as 2 Sydney bank clerks told me you could, as my body at the moment is nicely tattooed mostly all of it, but can you let me know if you will draw up papers to have it done legally by post, or if it can't be sold for a few £s now, so I can carry on to be the Most Beautifully Tattooed Man of Australiasia, if you won't offer me a price for it, will you be as kind to let me know right away if I can will it, at my own request, to have it desected in any way you think at my death later on, I am 27 years old now.—Your's truly, — —.

* * *

For a tired pædiatrician on holiday it was a joy to come on this concluding sentence in a paper on the epidemiology of streptococcal infections in infants: "Perhaps someone will be able to repeat these results in humans."

Digitized by Google

Letters to the Editor

CHRISTMAS GIFTS

SIR,—I appeal once more to members of the medical profession to help those who are dependent on others for extra comforts. The beneficiaries of the Royal Medical Benevolent Fund are in such a case. They are either aged or infirm practitioners, their wives, widows, or children, and, through no fault of their own, find themselves in need of help.

I hope that subscribers to the fund will send donations to provide a little extra cheer at Christmas time, and I earnestly beg those who are not subscribers, not only to send Christmas gifts but to become regular supporters of the fund. A special effort to obtain new subscriptions is urgently necessary because certain medical bodies, such as the panel committees, which used to make generous contributions, have gone out of existence with the National Health Service Act.

Donations and subscriptions, marked "Christmas Gifts," should be sent to the Secretary of the Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, and will be gratefully acknowledged.

WEBB-JOHNSON
President, Royal Medical Benevolent Fund.

EXSANGUINO-TRANSFUSION IN ACUTE LEUKÆMIA

SIR,—Dr. Maycock (Sept. 18) does not understand on what grounds I made the statement that "it is impossible to obtain very large quantities of blood at any one time in England." My reason was a simple one: the attempt was made and was unsuccessful. True enough, I did not apply to any of the regional transfusion centres: I left that to a junior colleague.

If Dr. Maycock had read my preliminary communication, he could not have failed to notice that I emphasised that, as far as is yet known, the beneficial effect of exsanguination-transfusion is only temporary; but, nevertheless, the fact that remission does occur suggests a number of fresh avenues of research.

I am, of course, grateful to Dr. Maycock for reminding me of the difficulty of getting certain groups, but I must assert that I am well aware of the elementary facts he so clearly sets out. It is, of course, true that the decision to try exsanguino-transfusion in acute leukæmia is always a difficult one; and, in fact, much of the onus has to be placed on the relatives. But what is meant by saying that "exsanguination-transfusions should always be deliberately planned in consultation with the regional blood-transfusion officer" I frankly do not know. Surely, it is the task of the physician to plan the treatment, always, of course, subject to the availability of the therapeutic agent—in the present case, blood.

London, W.1. A. PINEY.

H. INFLUENZÆ MENINGITIS TREATED WITH STREPTOMYCIN

SIR,—There are two statements in Dr. Smythe's otherwise admirable paper of Sept. 25 which may lead to some misunderstanding regarding the value of penicillin treatment in this condition. On p. 485 he writes, with regard to the 12 cases referred to the London Hospital for streptomycin treatment: "In 10 of them penicillin or sulphonamides had been administered before admission; but these drugs had not controlled the infection and *H. influenzæ* was still present in the cerebrospinal fluid or blood." Page 490 contains the statement: "Though penicillin combined with sulphonamides does not appear to be so effective as streptomycin it may yet prove useful in combined therapy."

From this it would appear (1) that adequate penicillin treatment had been given to 10 of 12 cases and that this form of treatment had failed where streptomycin succeeded; and (2) that combined penicillin-sulphonamide treatment is inferior to streptomycin therapy either alone or combined. Neither of these assumptions is substantiated in Dr. Smythe's or any other paper published hitherto. As regards (1) it is evident from the case-histories given that 7 out of the 8 cases previously treated with penicillin had been given either no intrathecal penicillin or intrathecal injections in inadequate amounts. The one case (no. 2) which had adequate penicillin-sulphonamide treatment was proved to have a sterile C.S.F. before commencing streptomycin therapy. It is an open question, however, whether in this case complete restoration of health might not have resulted if streptomycin treatment had been started earlier in the illness.

This comment is not intended to make a case for combined penicillin-sulphonamide treatment as against streptomycin therapy either alone or combined. All one is justified in saying at this juncture is that there seem to be special merits in each of the proposed forms of treatment. Further comparative work appears necessary for the evaluation of and the definition of indications for the various methods of therapy now available.

K. ZINNEMANN.

Bacteriology Dept., School of Medicine, Leeds.

PROPRIETARY MEDICINES UNDER THE ACT

SIR,—Mr. Godding's article of Sept. 18 (p. 465) is interesting, but it leaves out many aspects of the case.

First, I believe that the machinery for investigating excessive prescribing under N.H.I. was prompted by the fixing of a total limit to the drug fund, and when the chemists' accounts rose above this figure they were only paid part. Consequently the chemists were particularly keen to see that the cost came down. Nevertheless, is there any evidence that this machinery has been abused and tended to prevent proper medical treatment? What about the cases on adrenal cortical extract running into hundreds of pounds per annum per case? In one of these cases the doctor wrote to the insurance committee before prescribing and was assured that he could order this. Consequently I feel that the manufacturers of proprietary preparations of the highest ethical standing of this type have little cause for apprehension.

But there is another class of preparation. The Chemists' Federation appears to be trying to impose standards on preparations it admits to its list, which are of course less rigid in the case of ethical proprietary preparations because the doctor is expected to examine their formulæ, &c., more closely than an uneducated patient would do. It does not, however, so far as I know, claim to have vetted all the previous inclusions to the list by the same measure, and, seeing that the federation was principally founded both for price-protection and limitation of sale of medicines to chemists, it cannot completely serve both masters—i.e., the trade and the medical profession. The question of standards should be dealt with by a separate body, free from criticism on this score, on the lines of the American Medical Association arrangement.

Personally I am more interested in the standing of the makers than in prescribing a proprietary article. If, for instance, I order sulphanilamide I do not mind whose make is supplied, provided it is a reliable firm possessing full facilities to ensure that the preparation is proper. I do not like a mixture of say quinine sulphate and quinine alkaloid being supplied for quinine alkaloid, whatever the explanation of the offending firm; but here we are getting off the question of proprietary medicines.

Nor do I like the guarding which still occurs in the formulæ of some proprietary preparations. I am referring to ingredients not in the *B.P.* or *B.P.C.* which on close examination appear to be extracts of mistletoe and the like. What evidence is there that they have any therapeutic effect?

The interest of the federation is to promote the sale of its members' proprietary articles. Is this the real interest of pharmacy? If practitioners are to be encouraged to prescribe proprietary preparations then there is little necessity for pharmacists to be properly trained, and it is in effect a further development of "multiple" pharmacy. Should the chemist be encouraged to keep the raw materials in stock so that he can make, on demand, the exact preparation required by the doctor, charging more for extemporaneous manufacture? Or should he make the patient wait and obtain the preparation ready finished from his supplier? The outcome of this argument is obvious, and is indeed partially

Digitized by Google

evident today. How many pharmacists make such things as Parrish's Food themselves?

Finally I would like to make a suggestion regarding future formularies. From the doctor's point of view a formulary covering the whole country has disadvantages. There was a tablet (tab. febrifuge) in the *North of England Medical Formulary* which was very popular. When the *National Formulary* came into being this tablet's name was first altered and later the strength was halved. Here tab. febrifuge are still ordered, and owing to this name being used on a prescription form the practitioner can get the original formula and the pricing office can deal with the prescription. So in any major alteration of formulæ I would suggest that a new name be adopted for the new preparation so that this can still be the case. I know this cuts across the present accepted views regarding naming (see preface to *N(W)F*) but I have outlined the practical reasons for this modification.

Seaham. A. FORSTER.

CHARMS

SIR,—Dr. Inman's observations (July 10, p. 77) remind me of a case encountered 6000 miles away.

In 1931, when I returned from Great Britain puffed up with the possession of a membership, a railway-ticket collector in my native town of Dadu, Sind, hearing of my recent exaltation, came to consult me. His face was covered with warts—more numerous about his chin, which made shaving an agony. His disappointment was as great as my chagrin when I told him that we, the English doctors, had not yet found a cure except by a knife or caustics which were out of question in his case. After about a month I happened to meet him again and was astonished to see that his face was completely clear of warts. I inquired the name of the remedy, and this is what he said. "Sir, after having seen that even the biggest doctor could not help me, I went to Kotri, a village about 100 miles away, where I had heard that an untouchable class of woman, 'Chuhri,' could cure my disease. She warned me that I would not be able to stand the ordeal, but I assured her that I would. On this she drank some dirty-looking water, gargled, and ejected it in a stream all over my face. Of course my repugnance was extreme, but not so great as my disappointment when you said that you had no cure. She repeated this process for three days, and at the end my face cleared up like magic."

Though amused by this story, I could not but feel humiliated; for the proof of pudding lies in eating, and I had eaten the humble pie.

Bellary, India. P. V. KARAMCHANDANI.

LETTER TO A NEPHEW

THE following is the final letter in this correspondence:

MY DEAR UNCLES,

I am very grateful for your friendly concern in my future and for the compliment you pay me in addressing me as a mature, level-headed, person. As such, I hope I may put forward my own views without appearing presumptuous or in any way unheedful of your counsels.

You will understand that I have no preconceived ideas whatever about working within or without a "service"; so I tend to remain unmoved by arguments which are based on these ideas. It seems to me, on the contrary, that a "service" will become what I and my colleagues make it, and that judgment might well be deferred until we have had our chance. In Sweden the profession have made a success of State-controlled medicine, and I see no reason why we should not do as well.

I agree with my old-fashioned uncle that any claim to a vocation would ill become me at this stage; at the same time, I feel that the job most worth doing would be one which most directly concerns itself with the public weal, and this implies ideals of a kind. They are, I hope, appropriate to my age and my capacity, and I shall be very happy to devote myself to their realisation as opportunity allows. I expect help rather than hindrance from the framework of the National Health Service; for, short of assuming that it is designed against the public weal, it must be intended as my servant, not my master. Its aims so far as I can gather, are the same as my own.

Forgive me, but what would you say if I suggested that any circumstance whatever might suddenly induce your own patients to regard you as mere "mechanisms" instead of the very able doctors you are? I take it that you ridicule the notion that any change of label or wrapping could affect the quality of your work in the slightest degree; please allow me to feel as unchangeable as you know yourselves to be. If the "practical" view cannot respect this deep conviction of mine, then I am afraid I feel bound to reject the practical view.

My solemnity must strike you as rather pompous, but I thought that I could thank you best by taking your remarks very much to heart and answering them with all the seriousness which I feel they deserve.

Your grateful and affectionate nephew,

CHARLES.

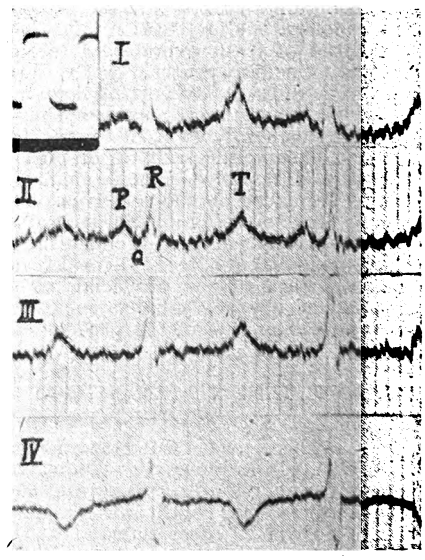
PRIVATE PATIENTS NOT ADMITTED

SIR,—The teaching hospitals, which have consulting-rooms available for their medical staff, provide an experience analogous to that of allowing private patients in health centres. This is how it works. A patient well known to me was sent a few days ago by her doctor to the hospital to see a consultant. There she was told that it would be three weeks before she could have an appointment. But she could be seen as a private patient if she liked to pay three guineas. As she was in a good deal of pain she consented, and the time was fixed for two days later. Incidentally, if she had gone to the non-teaching hospital, which was nearer to her home, she would have seen a better man without delay or the payment of any fee.

LAY OBSERVER.

DIAGNOSIS AND TREATMENT OF PANCREATIC NECROSIS

SIR,—An electrocardiogram on the sixth day of acute pancreatic necrosis, which had been recognised as such during the patient's life and confirmed by necropsy, showed a pronounced elongation of the Q–T interval (Q–T = ½ sec. with the pulse-rate 80 per min.), an increased T deflection, and a slackening of the heart's action, without any distinctive signs of damage to the heart muscle (see figure), a type of electrocardiogram which is usually described as tetanic. Thinking that these electrocardiographic changes might be due to a lowered blood-calcium level as they are in tetany, I decided to check this in the next case of pancreatic necrosis, and found both the altered electrocardiogram and a lowered blood-calcium level as expected. The patient was treated with intravenous injections of a 10% solution of calcium gluconate 10 ml. twice daily, controlled by estimation of the blood-calcium level. She began to improve continuously from the first day of treatment and recovered within three weeks.



The lowered blood-calcium level I attribute to the binding of the body calcium at the foci of fat necrosis and to the lack of absorption of calcium from food because of persistent vomiting. I suggest that the formation of foci of fat necrosis causes a lowered blood-calcium level, which in turn intensifies vagal tonus, producing an elongated Q–T interval, increased T deflection, and slowing of the heart. The more numerous and more extensive the foci of fat necrosis, and the faster the rate of their formation, the more pronounced will the electrocardiographic changes be. Consequently electrocardiography coupled with the determination of the

Digitized by Google

blood-calcium level may be of value in the diagnosis of pancreatic necrosis. The restitution of the normal blood-calcium level in patients with pancreatic necrosis by intravenous injections of calcium seems to be indicated.

Lublin, Poland. S. E. LUCZYŃSKI.

COMPENSATION FOR PRACTICES DEPLETED DURING WAR SERVICE

SIR,—In 1939 many general practitioners conceived it their duty to join the Territorials or the Volunteer Reserve of the Royal Navy or the R.A.F., in readiness for an expected blitzkrieg. During their service they lost very heavily financially. The pay of a lieutenant (or flying-officer) was about £380 a year, of a captain (or flight-lieutenant) about £430, and of a major (or squadron-leader) about £640, plus small marriage allowances where applicable. Many had heavy civilian and family commitments to meet.

They returned in 1945 or 1946 to practices which were sadly depleted (unless they were fortunate enough to have partners to look after their interests while they were away). In many cases there has been only one full accounting year since their return; in no case can there have been more than two years. For purposes of compensation, therefore, it would be seriously wrong to assess the value of their practices on these difficult first years of the post-war re-start.

It is understood that such cases will be specially considered; but they are so numerous, and so obviously entitled to fair play as a right and not as a concession, that some general principle should apply. I submit that the only fair assessment is to take the pre-war value of the practice, and to add to it a proportion equivalent to the average increase from 1939 to 1947 of the value of the practices of those who, for good or bad reasons, remained behind. This proportion could easily be got out by the tax authorities, but I estimate that it is about 70%.

Only so can these men who have been penalised for their war service by loss of income escape being further penalised for that service by assessment of their life's savings at figures which bear no relation to what their position could have been had they ignored the call in 1939.

PRE-WAR V.R.

HOW MANY NURSES?

SIR,—Your leading article of Sept. 25 deals with certain problems raised in my report on the nursing services.

I venture to suggest that you have failed to appreciate an essential point in the argument in chapter IV of my report. This point is that the absence of any demonstrable correlation between the nurse-patient ratio and duration of stay in, say, tuberculosis sanatoria in no way invalidates the criterion I have adopted of duration of stay as an index of nursing (or medical) effectiveness. Nor does it destroy my hypothesis. Just as the presence of correlation between these variables in general hospitals may be taken to indicate the effectiveness of nursing care in these institutions, so the absence of correlation in sanatoria may be taken to indicate a corresponding ineffectiveness of nurse training or treatment in sanatoria. Consequently, it is, I submit, incorrect to speak, as you do, of "conflicting evidence" or "equivocal results". On the contrary, all the results seem to me to be concordant. Nor is it correct to say that the "only" evidence relates to general hospitals. The fact that the data—the latest available in published form—refer to 1938 is beside the point.

You say that few will agree with the assumption that duration of stay is an objective measure of the task of nurses and doctors, because duration of stay is also affected by other variables—viz., type of illness, facilities for investigation and treatment, pressure of waiting-lists, provision of convalescent homes, and quality of diet. Is this not rather like arguing that we cannot judge the health of school-children by their stature, because stature is also affected by hereditary and other factors? My contention (see para. 89 of the report) is that there should be a functional dependence of duration of stay on staffing ratios when all other factors are held constant. I had hoped that this would be abundantly clear from the text. To pursue the analogy, this would be like saying that the stature of school-children is a measure of their health when hereditary and other "disturbing" factors are controlled. Furthermore the report gives consideration to the possible effect of "other" factors which your article implies have been overlooked. Indeed, where data are available, evidence is adduced to show that some of these factors (e.g., types of illness) have no apparent effect on the calculations.

Lastly, may I add that that it is no criticism to say that no solution is offered for the immediate nursing shortage. Our terms of reference explicitly excluded short-term palliatives and were confined to long-term measures.

Dept. of Social Studies, The University, Leeds. JOHN COHEN.

DIAGNOSIS OF PEPTIC ULCER IN GENERAL PRACTICE

SIR,—The possibility of successful treatment of peptic ulcer varies inversely with the chronicity; hence early diagnosis is most important. In the incipient stages the clinical picture is not always clear-cut, and it is not always practicable, particularly in industrial and in rural practice, for the family doctor, to whom these cases usually come first, to submit each one to radiography, which moreover at this stage is often negative or inconclusive. To meet this difficulty I have for many years used the Gregersen[1] benzidine slide test (G.S.T.) for occult blood in the fæces. It is a modification of the usual laboratory benzidine test in which it is claimed that the sensitivity is reduced so that the ingestion of hæmoglobin-containing food in normal amount does not produce positive results. It is as simply and rapidly carried out as are the usual tests for sugar and albumin in the urine, and is therefore eminently suited to general practice.

When in 1941 supplementary rations were granted for peptic-ulcer patients the opportunity was taken to investigate fully, including the G.S.T., those patients not previously examined who now applied for the requisite forms. My partner and I (the population is mainly industrial) thus made a fairly comprehensive survey of our patients with symptoms of peptic ulcer and other pathological conditions of the alimentary tract.

All cases diagnosed during the past ten years, in which both X-ray and G.S.T. findings are available, have been collected and analysed. There are 123 cases: 102 of peptic ulcer, and 21 of other alimentary conditions. I have omitted all cases of neoplasm in which on first examination the diagnosis was beyond doubt, and I have included a few ulcer cases diagnosed before the period under review, in which there are still active symptoms.

The G.S.T. findings have been compared with the X-ray and clinical findings, including in some cases confirmation after operation. Both the G.S.T. and X-ray findings were positive in 69 (68%) of 102 ulcer cases, and in 18 (86%) of 21 other conditions. The G.S.T. was positive and the X-ray findings negative, but clinical observations and subsequent history confirmed the positive diagnosis, in 19 of the 102 ulcer cases and 3 of the 21 other cases. The G.S.T. was negative, and positive X-ray findings confirmed the clinical findings, in 14 of the 102 ulcer cases, but in none of the 21 other cases. Thus there were 22 cases which might have been missed if the G.S.T. had not been used, and 14 cases in which the G.S.T. did not support the diagnosis.

In more than two-thirds of all cases both the G.S.T. and the X-ray findings were positive. Of these 87 cases, all but 22 were first diagnosed with the G.S.T. Where the two tests gave differing results, the G.S.T. was right rather more often than the X-ray findings: 22 cases and 14 cases respectively. Of the 19 ulcer cases with initial negative X-ray findings, 3 cases radiographed again after an interval because of a persistently positive G.S.T. gave a positive result, and 2 cases, one of neoplasm and the other of diverticulitis, both of them with initial negative X-ray findings and re-examined for the same reason, subsequently gave positive X-ray findings. These 5 cases are perhaps among the most significant in the series.

1. Gregersen, J. P. *Ugeskr. Laeg.* 1916, 78, 697, 752, 1197, 1260.

Digitized by Google

As regards ulcers only, both tests agreed in two-thirds of the cases; radiography failed in slightly under 1 case out of 5, and the G.S.T. in slightly less than 1 out of every 7 cases. For the other diagnoses the numbers are too small to give more than a strong indication: 11 cases of neoplasm; 5 which exhibited diverticulosis radiologically and had a positive G.S.T. (presumably cases of diverticulitis); and 1 case each of ulcerative colitis, regional ileitis, torsion of the cæcum, spastic colon, and pernicious anæmia.

Some clinicians still believe that, even with the G.S.T., hæmoglobin-containing food should be excluded from the diet for three days before the test. Maclean [2] strongly disagreed, and Ogilvie [3] found that, though meat in the diet might occasionally cause a faint colour with the G.S.T. after 30 sec., a blue or blue-green colour appearing within 30 sec. was proof of the presence of occult blood in the stool irrespective of the patient's diet, provided it had not included foods with a high blood-pigment concentration, such as black pudding, liver, and bone-marrow. However, because opinion on this matter is not unanimous, patients in this series were asked to abstain from meat-containing food for three days before bringing a specimen for examination.

The G.S.T. is performed as follows:

Powders are made up containing 0·2 g. of barium peroxide and 0·025 g. of pure benzidine. Put up in waxed paper they will keep indefinitely. Since different makes of reagent give various results, I have used benzidine 'AnalaR' (B.D.H.), which is specifically tested by the manufacturers against a freshly prepared 1 in 100,000 solution of blood. For the test one powder is dissolved in 5 ml. of a 50% solution of acetic acid 'AnalaR.' With a glass rod a small piece of fæces is taken from the centre of the stool and smeared on to a clean glass slide or a piece of white tiling. A few drops of the solution are then run on to the smear. A blue or blue-green colour develops within a minute if the test is positive, and the reaction is graded according to the depth of the colour and the time it takes to develop. Gregersen recognises three grades: +, a pale blue or green colour within 60 sec.; ++, a definite pale blue in 12–15 sec.; +++, a deep blue within 3 sec. Any colour developing after 60 sec. at normal room temperature is disregarded.

The patient is asked to bring a sample of fæces about the size of a bean or a pea, in a clean small jar. The test can then be performed in a few moments during the consultation. The powder, if preferred, can be made up in bulk. In a dark airtight bottle it will keep without deterioration for at least six months. I have tested the powder after that period, and found that it still gave a positive reaction in a 1–70,000 dilution of blood in water. For those doing the slide test for the first time it is advisable to have each powder made up separately till some idea is gained of the quantity needed for each test. It does not take long to learn the approximate quantity required and to tip it into the test-tube either directly from the bottle or with the tip of a spatula. There is no soiling of test-tubes with a fæcal suspension, and since only a small smear of fæces is used it can be easily cleaned from the slide with cotton-wool. In carrying out the test I have found the slides used by bacteriologists for examining hanging-drop cultures most useful.

To avoid so far as possible contamination of the specimen by blood from the rectum, anus, or vagina, it is wise to remove the portion of fæces for examination from the inside of the stool. Should it be necessary to examine fæces at once, some can almost always be immediately obtained by digital exploration of the rectum.

In estimating the value of the G.S.T. it is necessary to consider both its advantages and limitations. For the general practitioner it can be a valuable measure in the early diagnosis and treatment of alimentary ulceration. By its use he can sift and control his dyspepsias with more assurance and a better knowledge of the underlying pathology. Often it may enable him to decide more quickly which case requires the more expensive and time-consuming forms of investigation. By taking appropriate measures till all occult blood has disappeared from the fæces, it may enable him to avert the more serious complications of hæmorrhage and perforation. The minimal amount of blood required to give a positive result varies from one person to another, so a negative finding must not be considered conclusive and should always be judged in relation to the clinical picture. A positive result is always significant; and, provided precautions have been taken to exclude extraneous sources of blood, an attempt must always be made to trace the cause of the bleeding.

Edinburgh. S. LIPETZ.

2. Maclean, H. Modern Views on Digestion and Gastric Disease. London, 1928.
3. Ogilvie, A. G. *Brit. med. J.* 1927, i, 755.

HANDLING OF FOOD

SIR,—Both Dr. Stanley Turner's letter of Sept. 11 and the correspondence in your issue of Sept. 25 show the need for cleanliness in the handling of food. If employers realised what damage can be done by the deplorable methods to which attention has been drawn they would undoubtedly do something about it. Their efforts, however, will be nullified unless education in food-handling is also given to their employees.

In the scheme we have in Guildford the voluntary efforts made by the employers and employees, in willing coöperation with the council, will it is hoped produce the most satisfactory results. We have frequent meetings between representatives of the health committee and the food traders, and their employees, and this allows full discussion, in open session, of the reasons for all we ask in the way of improvement of methods and better sanitation in the premises. A representative of the particular food trade is always present to assist with the formation of the code of practice for his trade, and in this way we can ensure that whatever we propose in the way of improved conditions is a practical proposition. Food-handlers are shown why cleanliness on their part is essential, and how strict attention to cleanliness protects the public they serve.

Guildford Hygienic Food Traders' Guild is thriving: every trader who complies with the requirements is given a certificate of such compliance and of membership of the guild, and every employee is given a button badge. By their certificate and badge the public can see that the food trader and his assistant know their job and know how to produce clean food in a cleanly manner. I feel sure that this is the secret of success in the handling of food.

The collaboration of the public is also essential so that no person suffering from a communicable disease deliberately contaminates glasses or other articles used for the consumption of food. Education of the public on these lines is urgently required.

F. A. BELAM
Guildford, Surrey. Medical Officer of Health.

SELECTED FOR INTERVIEW

SIR,—In the past, candidates selected for interview for posts in either voluntary or municipal hospitals have invariably been allowed reasonable out-of-pocket expenses as well as train fares, when the distance travelled to the place of interview warranted such payments. Indeed some local authorities made use of a fixed scale of subsistence allowances based upon the number of hours of absence from home. It now appears that, under the National Health Service regulations, "there will be refunded to candidates their third class railway or bus fares where they exceed five shillings. *In no circumstances can subsistence expenses be paid.*" (I quote the actual words from a recent letter received by myself.) A brief study of your advertisement columns, together with a "Bradshaw," makes it obvious that many candidates may be away from home for twenty-four hours or even longer, assuming that they are usually selected from several of the main teaching centres. This latest form of economy is particularly mean since the majority of vacant posts are in the house-officer and junior registrar class, and the candidate for such posts can usually ill afford to be out of pocket, especially if he fails to be appointed.

Secondly, there is considerable, and to my mind quite unnecessary, delay in informing candidates for more senior posts when their applications have been unsuccessful. At present this delay may be anything up to two or even three months from the closing date for applications. The usual practice appears to be that candidates who have not been selected for interview

Digitized by Google

are not told until after the final appointments have been made. It would avoid much unnecessary suspense if unsuccessful candidates could be informed as soon as the short list is selected.

May I also make a plea for a little thought and consideration towards the candidate, whose time, after all, may be just as important as that of the interviewing committee. I was recently summoned for an interview by telegram and letter, both of which were dispatched forty-eight hours before the time of the meeting, but seven weeks after the closing date for applications. I happened to be on holiday at the time and received both communications approximately two hours before I was due to appear; but as I was in Scotland and the interviewing committee was in Southern England we were unable to meet. On another recent occasion I was kept waiting, with the other candidates, for two hours after the time arranged, because the chairman of the committee failed to turn up!

REGISTRAR.

MUMPS WITH SEVERE COMPLICATIONS

SIR,—That one general practitioner should meet with two consecutive cases of mumps with grave complications within three weeks is rather extraordinary. Both cases were treated at home.

CASE 1.—A clerk, aged 36, developed bilateral salivary adenitis on July 18, 1947. Five days later he had left orchitis and epididymitis with considerable constitutional symptoms, which increased in severity throughout the day. On July 23 he developed violent headache, slight delirium, severe abdominal pain, and half-hourly vomiting, with blood and mucosa in the vomit.

On examination the patient was very ill and unresponsive with yellowish conjunctivæ, temperature 105·2°F, pulse-rate 124, respirations 24 per min., nothing abnormal in the chest, and tender abdomen, especially the left hypochondrium. The urine gave a green deposit with Benedict's solution.

Acute pancreatitis was diagnosed. All attempts to give fluids by mouth failed. Vomiting persisted. Pethidine 100 mg. and hyoscine gr. $^1/_{150}$ were given, without producing any relief.

On July 24 his general condition was much worse, and he was restless with very severe abdominal pain; left testicle much bigger; delirium more continuous; temperature 104·2°F. A drip infusion of 5% dextrose in normal saline solution was set up through a Hamilton Bailey cannula into the right saphenous vein. Improvement in the general condition was noted within an hour of starting the drip. No urine was passed that day. The evening temperature was 103°F. 'Omnopon' gr. $^1/_3$ and scopolamine gr. $^1/_{150}$ were given twice during the night, with great relief and reduction in restlessness.

On July 25 the patient had had a quiet night and improved much in his general condition. Temperature 101°F. The patient passed urine. A litre of 5% dextrose was given and a second litre, of 10% dextrose, was begun. The patient started to take water by mouth. Vomiting ceased. By evening the second litre of dextrose solution was finished. A pint of concentrated red cells (supplied by the South London Blood Transfusion Service, Sutton) was given, and the cannula was removed. There was no abdominal pain or headache. Temperature 101·2°F, pulse-rate 86. The patient was drinking well. 'Sodium amytal' gr. 3 was given at night.

On July 26, after a good night, the patient's temperature was 98·8°F. Thereafter recovery was rapid and uninterrupted, except for thrombosis of the saphenous vein. Since 10% dextrose was the only solution available for the second litre (though this is twice as strong as what I normally use) the risk of venous thrombosis had to be taken.

CASE 2.—A pipe-layer, aged 26, was seen on Aug. 5, 1947, with bilateral salivary adenitis. He was not very ill, and two tablets of aspirin and opium were prescribed. Next day he had right orchitis and epididymitis, with a great increase in general malaise. Temperature 103°F. A suspensory belt gave relief. On Aug. 7 the temperature was 103·2°F, and the testicle was more comfortable, but the patient complained of abdominal pain, a severe headache behind the eyes, and generalised myalgia.

On examination the right inguinal region was tender, but the abdominal wall was lax and not generally tender.

On Aug. 8 the patient began to vomit and the retro-ocular headache became unendurable, making him weep and at times shriek out. He had intense photophobia, and two mild jacksonian fits. Nothing abnormal was found in the abdomen and chest. Neck rigidity was present, and Kernig's sign positive. The pupils reacted to light, but there was bilateral nystagmus. Temperature 103·6°F, pulse-rate 84. Meningo-encephalitis was diagnosed. Drinks of 5% glucose in small amounts were given. Omnopon gr. $^1/_3$ and scopolamine gr. $^1/_{150}$ half intravenously and half intramuscularly were given, with immediate relief. In the evening the patient was crying with headache, and nystagmus was increasing; he had another fit, with momentary loss of consciousness. Temperature 104·4°F, pulse-rate 68. Omnopon and scopolamine were given subcutaneously.

On Aug. 9 the patient had had six hours' sleep during the night, but the headache was again as intense as ever, and he was vomiting, not drinking, and passed no urine. Temperature 98·2°F. Potassium citrate was given two-hourly. Photophobia increased. Blackout curtains were put up, and two scarves were placed over the patient's eyes. He shrieked if a chink of light showed under the scarves. Lumbar puncture showed the cerebrospinal fluid (C.S.F.) to be under pressure of 160 mm. H_2O; 10 ml. was withdrawn. This was followed by immediate relief. Within ten minutes the scarves were removed from the patient's eyes, the curtains were drawn back, and the patient chatted happily. The C.S.F. contained 12 lymphocytes per c.mm., the other constituents being within normal limits. The patient made an uninterrupted recovery.

Interesting points are: (1) the severe constitutional symptoms in both cases as soon as the testicle was affected; (2) the fact that both patients had orchitis as a prelude to much more grave complications; and (3) in the second case, the fact that, after the fever had dropped by crisis, the symptoms of intracranial pressure increased, and responded dramatically to lumbar puncture.

Haywards Heath. H. DERBYSHIRE BROWNE.

SUBACUTE BACTERIAL ENDOCARDITIS

SIR,—I read Professor Bramwell's article of Sept. 25 with interest. No doubt the most important factor in the prognosis, apart from penicillin, is the duration of the disease. Professor Bramwell and recent American workers have stressed this. I think the lack of close correlation between the in-vitro sensitivity of the organism and the dosage required is intimately related to the duration.

It is well known that small doses of penicillin will rapidly clear the blood of streptococci, and the mechanism is probably a bacteriostatic action associated with circulating antibodies and phagocytes. In the vegetations, which consist of relatively avascular and necrotic masses of platelets, fibrin, and streptococci, penicillin must act predominantly as a bactericidal agent. Obviously, the duration of the disease will largely determine the size and extent of these vegetations, and thus indirectly the dosage necessary. There can be no fixed dosage schemes in the treatment of this condition.

We have at present two cases in hospital who are being given one million units three-hourly for six weeks.

General Hospital, Birmingham. M. J. MEYNELL.

A DIPLOMA IN VENEREOLOGY

SIR,—Like many others from distant countries of the British Commonwealth, I came to Great Britain for postgraduate instruction and additional experience in venereology. Although I have studied, worked hard, acquired knowledge, and gained experience under some of the best teachers of this country, it seems that I must eventually return without taking an examination for a diploma in this particular subject.

Almost every other branch of medicine has some special qualification obtainable by examination—e.g., D.C.H., D.I.H., D.P.H., D.T.M. & H., D.OBST. R.C.O.G., D.P.M., D.M.R., D.BACT., D.O.L., T.D.D., and D.O.M.S. I submit that the institution of such a diploma in venereology would help to raise the standards in a subject which has been greatly neglected by the profession, and whose importance has been shown repeatedly in peace

Digitized by Google

and in war in terms of individual suffering and loss to the community. The need for such a qualification for students from distant lands (Empire as well as foreign) is an additional argument for its institution.

London, E.1. OVERSEAS STUDENT.

TECHNIQUE OF DISCUSSION

SIR,—Some of your readers may like to hear about the conclusions reached at a session of the Sensory Summer School devoted to the subject of democratic discussion. It was agreed that when any committee or other group meets with the aim of reaching agreement on a controversial subject the following improvements on the accepted technique are desirable:

1. That in the initial phase of controversial discussion it is essential to remain receptive to new suggestions and innovations and to treat them from the viewpoint of consolidating and elucidating them before allowing negative criticism, thus enlarging the field of possibly relevant thought.

2. That the method of proceeding by argument around concrete resolutions and their amendments or counter-amendments should be recognised as inefficient and time-wasting. A resolution should be treated as fluid the moment any controversial amendment is proposed, and decision by majority vote should be deferred, if not eliminated, by a readiness to reformulate the subject at issue in terms which may facilitate agreement.

3. That in wording motions it is advisable to avoid both emphatic negatives and positive superlatives which have the effect of ruling out possible alternatives (e.g., phrases such as "The most important point is. . . .").

4. That if opposing sides in a conflict are asked to state all positive elements in their attitude, deadlock may be avoided; or, if deadlock has already been reached, solution may be found by the same method.

5. That every effort should be made to build up a strong tradition of individual self-discipline in discussion, based upon a feeling of responsibility for reaching agreement, keeping in mind at all times the need for positive and relevant statement.

The meeting concluded that any group of people concerned with matters of social organisation or government must, in order to be efficient, both make exact and definite statement of its principles, and at the same time provide methods of continuous self-criticism, developing and re-stating those principles in new terms. A single group rarely, if ever, can fulfil adequately both these functions. An experiment now in progress seems to show that an effective way of doing so is a dual organisation; there should be an executive body dealing with short-term policy and matters of urgency, unhampered by full responsibility for long-term considerations and wider issues, while a sensory body dedicates itself to the deeper implications of truth, principle, and long-term policy. In order to ensure the smooth working of their mutual relationship, the executive should refrain from limiting the scope of the work of the sensory body, and the sensory body should refrain from advising what action should be taken by the executive.

London, W.1. J. N. GLAISTER.

IMMUNISATION AGAINST WHOOPING-COUGH

SIR,—It might be of interest to some of your readers to know that I have seen, in the past twelve months, doing outpatient work at hospital where quite a large number of babies and children have gone through my hands, no cases of whooping-cough. This is attributed in Vancouver to the immunisation against diphtheria and whooping-cough during the period from six months to a year, although of course some children are immunised later. The injections used are made by Connaught Research Laboratories and certainly appear to be highly efficient. When one remembers that the infant mortality for Vancouver varies from 24 to 30 possibly the absence of whooping-cough is a contributing factor.

I thought that your readers would be interested to hear that the absence of whooping-cough is attributed by the pædiatricians to these injections.

Vancouver General Hospital, Vancouver, B.C., Canada.

DONALD PATERSON
Pædiatrician-in-Charge, Health Centre for Children.

Public Health

Plumbing in America

AN officer of the Building Research Station has been to study plumbing practice and research in the United States, and the Department of Scientific and Industrial Research has published a record of his visit.[1]

The "one-pipe" system, in which the waste pipes from sanitary fittings of all kinds discharge into a common pipe directly connected to the drain, is so well established in America that it has ceased to be the subject of controversy there. But there are considerable variations in its practical application: for example, in two large cities, Philadelphia and Baltimore, special anti-siphonage ventilation pipes may be omitted altogether where each individual waste pipe runs independently to the soil-waste stack; and elsewhere various degrees of special ventilation are required.

HAZARDS

Contamination of drinking-water due to cross-connexions and back-siphonage into water lines has had much attention since the epidemic of amœbic dysentery in Chicago in 1933, when 1400 people were ill and 98 died through drinking water contaminated in two large hotels. Investigation has revealed many cases of water being rendered unsafe after arrival in the plumbing system of a building, and ill health has often been shown to be directly attributable to "pollution in the plumbing." In consequence, certain plumbing practices at one time normal in America have been amended. Speaking generally, those found dangerous are:

(*a*) Any cross-connexion between a supply of potable water and a supply of unpotable water by means of a valve of any kind. The more serious cases have arisen where the unpotable water was sewage. There have been cases of potable water-supplies being used for flushing drainage pipes by means of a value connecting the water-supply and sewage systems. The hazard in any such case of "cross-connexion" is that if the valve is opened, or fails to give complete closure, at a time when the pressure on the polluted water side of the valve happens to exceed that on the potable water side, the potable water will become contaminated.

(*b*) Any case where water is supplied to a washing or sanitary appliance, or other water-using device, in such a way that the outlet of the supply—e.g., the outlet of a tap or of any extension pipe attached thereto—is below the level to which waste water in the receiving vessel may rise. (In determining this level account must be taken not only of normal usage but also of exceptional conditions such as stoppage of an overflow channel. Hence the level to be considered is that at which water would begin to flood over the top edge of the appliance.)

The way in which hazards to health arise in the case of simple cross-connexions has already been noted. The hazard associated with the "submerged" or "underwater" inlet, is as follows:

Negative pressures necessarily occur from time to time in the water-supply systems of buildings. For example, if the stop valve controlling the supply to a building is closed while repairs are in progress, any water drawn from the system on the house side of the stop valve must come from the water remaining in the pipes, and as this water falls it induces a negative pressure of air in some part of the pipes. If there is any submerged inlet it may, by reason of the negative pressure in the pipes leading to it, siphon out waste water from the appliances which it serves. For this to happen, the control tap at the submerged inlet must either be left open or be not completely airtight; but there are many circumstances in which taps may be left not completely closed, and certain water-control devices would in any case permit water to pass through them in a reverse direction. If the water in the appliance served by the submerged inlet happens to be

1. Plumbing in America. National Building Studies: Special Report no. 2. H.M. Stationery Office. Pp. 24. 6*d*.

Digitized by Google

contaminated, the water drawn off in due course from various taps in the building, or even in neighbouring buildings, will be polluted. Even if the stop valve is not closed, pollution may take place if any leakage or draw-off in the system or in the mains has the effect of robbing certain taps of water.

The action which has been taken to deal with these water-contamination hazards has included: (*a*) correction of the defects, if practicable, wherever found; (*b*) amendments to plumbing codes and special regulations regarding cross-connexions and back-siphonage.

It may be asked whether our own plumbing systems and appliances may give rise to similar hazards to health. The following points may be considered:

(*a*) Cross-connexions between potable and unpotable water are not approved in our practice, but it may not be correct to say that none exist.

(*b*) The more serious back-siphonage hazards in America are due to the combination of flushing valves with mains supplies. The flushing valve is comparatively rare in this country and only some of our areas permit mains supply to all taps. It happens, however, that in those areas where water is plentiful and can be supplied to taps directly from the mains, flush valves are normally more acceptable because there is less concern that they may waste water. Any developments for the increased use of flushing valves, particularly when coupled with the use, or greater use, of mains supply, seem to call for careful thought.

(*c*) The development of new water-using devices gives concern in America, lest the hazards of back-siphonage, &c., should be introduced. Similar care is needed here, and an assurance that existing appliances, particularly in hospitals, are above reproach from this point of view.

(*d*) Although low-level inlets for baths and the like are no longer regarded as good practice in this country, it is common to locate tap inlets below the flood rim, though above the overflow. It is very difficult to estimate the degree of hazard, if any, arising from this practice. Repeated inquiry was made in America as to the incidence of cases of contamination which could be definitely attributed to tap outlets being above the overflow only. The answer was usually, "We have no data of this kind. It is not possible, except by chance, to relate illness to such a cause because back-siphonage is intermittent and it may pollute the water system, and lead to the drinking of unsafe water, some time later—even in another building. One can only proceed on the basis of the probability that sooner or later an arrangement which can be shown to permit contamination in an experiment which simulates the conditions of practice will actually take place in a plumbing installation. The remedy is so simple and cheap that it should be applied."

THE TOILET

The Central Council for Health Education has stated that in this country every year there are over 5000 deaths from diarrhœa and dysentery and that many of these deaths are no doubt caused by the almost universal habit of not washing the hands after urination and defæcation.

In America, in hotels and restaurants of various grades, in railway trains, railway stations, cinemas, &c., the sanitary equipment of toilet rooms was generally noted to be of a higher standard than in this country. Lavatory basins, with the important accessories of towels and soap, were nearly always to be found close to the water-closet. Soap was most commonly provided through a small ejector in the form of a spring tap: several pressings of this tap are needed to get enough soap for washing, and there is therefore little encouragement to waste. Towels were more usually of paper folded in packs (often in special containers designed to discourage waste) and it was rare to find supplies exhausted. A device to provide cloth towels in such a way that they could be used but not removed was as follows:

The towels, packed in a neat pile, each had a chain attached to one corner. The other end of this chain was connected to a ring which passed over a rod running down into the used towel basket. On being released after use the towel fell automatically into the basket.

There are very few public conveniences in America, and it is normal practice for the public to use the toilet rooms of hotels, automobile service stations, &c., whether they are at the time customers of these places or not. This arrangement has advantages as well as disadvantages. In Britain, where hotels do not normally welcome non-patrons in their toilet rooms, the public conveniences are rather irregularly distributed and difficult for the stranger to find; they are often closed when needed, and seldom offer the same inducements to hand-washing after toilet.

Some differences between American and British plumbing appliances and fittings are instructive. The superior flushing of American closet pans merits attention. American practice usually favours cisterns for houses and valves for the larger buildings.

SOIL STACKS

Because of the severity of winters in America, soil stacks in that country are located inside buildings, whereas in Britain they are normally placed outside in order to give greater safety in the event of leakage. Some trouble has occurred in America due to leakages from internal soil stacks but almost no anxiety is felt about them in modern buildings in view of present-day standards of plumbing labour. Perhaps if similar confidence were justified in this country generally, there would be less opposition from sanitarians to internal pipes and concealed pipework.

Food and Drugs (Milk and Dairies) Act 1944

Owing to legal difficulties the Minister of Health will not after all be able to bring this Act into operation this year; in the meantime he asks authorities to renew licences under the Milk (Special Designations) Regulations for the year 1949.

Health in the Second Quarter

The quarter ended June 30, 1948, was remarkable for having the lowest infant-mortality rate (31 per 1000 live births) and the lowest stillbirth-rate (22·7 per 1000 total births) for any quarter on record and the lowest death-rate (10·3 per 1000 total population) for any June quarter. The birth-rate, which like the death-rate is based on the 1947 total population, was 19·0 per 1000, compared with 18·9 in the previous quarter, 21·9 in the June quarter of 1947, 19·1 in June, 1946, and an average of 17·5 for the second quarters of 1942–46. Births exceeded deaths by 93,355, not such a great excess as in 1947, but greater than in 1945 or 1946. Marriages totalled 183,954, which was 6000 under the five-year average. The Survey of Sickness revealed that in January, February, or March this year 67·2% of the people interviewed were either ill or injured, but the loss of work averaged only 1·1 days per month.

Notification of Infectious Diseases

ENGLAND AND WALES

Disease	Week ended Sept. 4	11	18	25
Cerebrospinal fever	29	26	26	26
Diphtheria	105	136	126	125
Dysentery	64	84	50	68
Encephalitis lethargica	1	2	1	1
Measles, excluding rubella	2962	2608	2614	2703
Ophthalmia neonatorum	42	53	47	36
Paratyphoid fever	11	32	17	15
Pneumonia, primary or influenzal	246	261	283	277
Polioencephalitis	3	4	2	3
Poliomyelitis	70	72	72	70
Puerperal pyrexia	94	79	101	87
Scarlet fever	734	833	925	1068
Smallpox	..	..	..	..
Typhoid fever	9	28	28	29
Whooping-cough	2996	2877	2635	2259

Digitized by Google

Obituary

ALEXANDER WILSON GILL

M.D. EDIN., F.R.C.P.

Dr. Wilson Gill died on Aug. 30, at the age of 60, in the North Staffordshire Royal Infirmary, where till his retirement this year he was in charge of the neurological and cardiological clinics and was senior physician.

He was educated in Edinburgh at the Royal High School and the University, graduating in medicine in 1909. After holding resident appointments at Addenbrooke's Hospital, Cambridge, and the City Infirmary, Birmingham, he obtained his M.D. Edin. in 1912 with a thesis on auricular fibrillation, and then settled in practice in Hanley as the partner of the late Mr. Reginald Alcock. During the 1914–18 war he served in France and Belgium, and when he was wounded showed the courage characteristic of his whole life. With the late Sir Arthur Hurst he became interested in the study of functional diseases in soldiers, and for a year he acted as neurologist at Seale Hayne Military Hospital. He was also assistant editor of the *Seale Hayne Neurological Studies*. On his return to general practice he successfully treated functional disorders by hypnosis.

In 1922 he was elected to the staff of the North Staffordshire Royal Infirmary, and after taking the M.R.C.P. in 1927 he undertook only consultant work. In 1944 he was elected F.R.C.P. His advice was sought particularly on functional as well as organic neurological states and cardiovascular diseases, but he never lost interest in general medicine. A colleague says of him that "he never failed to give comfort to his many patients, both in the lay and medical world. He had a keen understanding and sympathy and imparted confidence with his fluent and explicit diction. There was never a more honourable, upright, and kindly man than Alec Gill, and during his last illness it was often said that he practised what he preached, for he made friends of his fears and faced a difficult situation with fortitude. A great lover of Johnson and Boswell, he spent his spare time either reading the classics or fishing. In his younger days he was a tennis enthusiast."

Mrs. Wilson Gill was formerly Miss Edith Mary Johnson, of Congleton.

Births, Marriages, and Deaths

BIRTHS

CURTOIS.—On Sept. 23, at Singapore, the wife of Lieut.-Colonel G. M. Curtois, R.A.M.C.—a son.

DOCKRAY.—On Sept. 24, the wife of Dr. J. V. Dockray, O.B.E.—a daughter.

HUMPHREY.—On Sept. 25, the wife of Dr. J. H. Humphrey—a daughter.

MARSHALL.—On Sept. 28, at Oxford, the wife of Wing-Commander A. B. Marshall, M.R.C.S.—a daughter.

STIDOLPH.—On Sept. 27, in London, the wife of Mr. Neville Stidolph, F.R.C.S.—a son.

TOBER.—On Sept. 28, in London, the wife of Dr. Archibald Tober—a daughter.

TURNER.—On Oct. 1, in Edinburgh, the wife of Dr. R. D. Turner—a son and a daughter.

WILLIAMS.—On Sept. 26, in London, the wife of Dr. R. E. O. Williams—a daughter.

YORKE.—On Oct. 2, in London, the wife of Dr. Allan Yorke—a son.

MARRIAGES

FRANCIS—WARREN.—On Sept. 9, at Bromley, Arthur Evans Francis, M.D., to Marian Elizabeth Warren.

INGRAM—FORBES IRVING.—On Sept. 25, at Montana, Switzerland, George Ilsley Charlton Ingram, M.B., to Patricia Margaret Forbes Irving.

MCKENZIE—BUCK.—On Sept. 30, at Birchington, James Alexander McKenzie, M.B., to Joyce Isabel Buck.

MAILE—KELLY.—On Sept. 25, in London, William Burgess Drayson Maile, M.D., to Mary Sheila Bridget Kelly.

PRITCHARD—LEE.—On Sept. 25, in London, John Pritchard, M.R.C.S., to June K. Lee.

WYPER—VERITY.—On Sept. 22, in Edinburgh, John F. B. Wyper, M.B., to Margaret Janet Verity.

DEATHS

AUBREY.—On Sept. 30, Harold Percival Aubrey, M.R.C.S., aged 66.

COSGRAVE.—On Sept. 30, Frederick Robert Cosgrave, M.D. Dubl.

NASH.—On Sept. 29, at Ashwell, Herts, Lorimer Gifford Nash, M.R.C.S.

SASS.—On Sept. 30, at Deal, Frederick Joseph Wilfrid Sass, M.R.C.S., D.P.H.

Notes and News

UNIVERSITY STIPENDS

LAST week Prof. C. E. Raven, D.D., in his address to the senate at the beginning of his second year as vice-chancellor of Cambridge University, discussed the growing discrepancy between the incomes which could be earned in the universities and in other professions. The University Grants Committee had lately pointed out that the maximum professorial salary which the Treasury recognises is £1450. If there was to be any ladder of promotion this meant that junior posts would hardly carry a living wage—certainly not a wage on which to marry and bring up a family. After six years of national service, men who held fellowships or junior teaching posts were being paid at the age of 30 salaries hardly larger than those offered in 1939 to men of 23. And these discrepancies would be aggravated, he pointed out, when the findings of the latest Spens report were implemented. For instance, the stipends of Cambridge professors did not rise above £1550, but a specialist appointed to the staff of a hospital was to be guaranteed a salary rising to £2500 at the 1939 value of money. "If the salaries of our own teachers of medicine are to be raised to the figures specified in the report," Dr. Raven continued, "we shall have anomalies in the scientific departments of the university which will not only be absurd but intolerable. It seems obvious that the University Grants Committee will have to reconsider the decision which it has at present upheld; or else we shall have to qualify for the medical school."

A SCOTTISH HOSPITAL

Dr. Gibson, the present medical superintendent, tells the story of the Dundee Royal Infirmary [1] from its lowly origin as a local dispensary about 150 years ago, describing its development into one of the finest institutions of its kind. Like all human institutions, it has had its vicissitudes; but it has always commanded the help of able and willing men and women. All classes of the community have contributed something to this, and some of Scotland's most distinguished physicians and surgeons have served on its staff. In Dr. Gibson the hospital has found a biographer as interesting as he is devoted.

VITRELLÆ

THE joint committee of the British Medical Association and of the Pharmaceutical Society of Great Britain which has been compiling a *National Formulary* has been seeking a convenient name for that group of therapeutic agents which are inhaled after crushing a small glass capsule. To distinguish these preparations from the "inhalations," and from the capsules intended to be swallowed, which form distinctive and quite different groups, the word "vitrella" has been chosen as being both precise and descriptive. It is proposed to use this title for this class of preparation in the formulary. Before long, therefore, we shall be ordering "Vitrella amylis nitritis min. 3."

THE B.P. 1948 EXPLAINED

A NEW pharmacopœia is scrutinised as carefully as the results of a general election—and the emotional accompaniments are not dissimilar. In the *B.P. 1948* new drugs and preparations are conveniently tabulated; and there are lists of those which have been relegated to another place (often the *B.P.C.*). But there is never a word about pharmacological actions—a double misfortune for readers unfamiliar with new official names, even though the compounds may be old friends in new guise. Discussion of the actions of drugs is still left to the writers of textbooks of pharmacology. In these difficult days, however, publishers of textbooks can rarely synchronise the release of new editions with the appearance of a new *B.P.*, even if authors would always coöperate. *The B.D.H. Guide to the B.P. 1948* is therefore particularly welcome. From this slender volume (pp. 145 + xiv) containing notes on the official monographs arranged alphabetically, the doctor or pharmacist can see at a glance whether a preparation is an old one, wholly or to all intents unchanged; an old one altered in strength or composition (*); or a new one altogether (**). When necessary a few words are added on pharmacological actions, and drugs which come under the D.D.A. or regulations or on the poison schedules are clearly indicated. The British Drug Houses Ltd. are to be congratu-

1. The Story of the Old Infirmary: Dundee Royal Infirmary (1798–1948). By H. J. C. GIBSON, M.D.

Digitized by Google

lated on producing this valuable booklet so promptly, and at the modest price of half a crown. It is a worthy successor to the *B.D.H. Guides* of 1914 and 1932.

University of Aberdeen

On Sept. 29 the following degrees were conferred:

M.D.—E. K. Cruickshank, C. E. Lumsden (with honours); J. A. McCredie Smith (with commendation).

M.B., Ch.B.—Eric McKay, W. G. Smith (with honours); Catherine C. Budge, Valerie A. Cowie, A. M. C. Duffus, G. P. McNair, Doris I. Manson, M. D. Paterson, Margaret P. B. Reid, F. G. G. Shepherd (with commendation); R. G. Blues, A. J. Booth, George Bruce, A. R. Burnett, R. F. Cant, G. T. M. Cummins, Wendy J. A. Davie, A. M. Donaldson, I. McI. Duguid, Leslie Dunbar, A. H. Duncan, G. D. Duncan, John Duthie, H. W. McG. Edwards, Margaret Farquharson, A. J. B. Gibb, Margaret G. Hay, G. A. Hendry, Margaret R. Inglis, A. G. Jessamine, A. G. Laing, Josephine M. Lomax-Simpson, A. H. Lorimer, A. C. MacDonald, I. A. McIntosh, W. T. D. McKenzie, Ian MacLeod, June M. MacTaggart, P. T. Main, Doreen Meldrum, Irene Milne, Joan M. Milne, J. C. Mitchell, Douglas Mortimer, T. D. Ness, Norna Pringle, H. G. Richmond, R. S. Ritchie, J. A. Shanks, Elma M. Simpson, Edith M. Skea, R. W. Smith, Elizabeth M. Somerville, Helen M. Sontter, Elizabeth M. Spark, Cecily J. M. Stewart, D. B. Strachan, Gillian R. Struan-Marshall, Audrey Sutherland, James Symonds, Elizabeth H. Thom, Margaret H. Thomson, James Wilkie, G. G. Younie.

Lloyd Roberts Lecture

On Thursday, Oct. 28, at 4.30 P.M., Mr. R. M. Titmuss will deliver this lecture at the Whitworth Street branch of St. Mary's Hospitals, Manchester. He is to speak on Parenthood and Social Change.

London Association of the Medical Women's Federation

The annual general meeting of the association will be held at the Royal Free Hospital School of Medicine, Hunter Street, W.C.1, on Tuesday, Oct. 12, at 8.15 P.M., with Miss Jocelyn Moore, the president, in the chair. (The ordinary notices have gone astray in the post, and members are therefore asked to accept this announcement.)

International Congress of Ophthalmology

A list of doctors practising ophthalmology in Great Britain is being compiled for the new Indicia in connexion with this forthcoming congress. All those who are *not* members of the Faculty of Ophthalmologists or the Ophthalmological Society of the United Kingdom are asked to send their names, qualifications, and addresses to the honorary secretary of the society, 45, Lincoln's Inn Fields, London, W.C.2.

Regional Hospital Boards

The Minister of Health has made the following appointments:

North-West Metropolitan.—Dr. W. J. T. Kimber, medical superintendent of Hill End Hospital, St. Albans (in succession to Dr. J. R. Rees).

Welsh.—Mr. E. K. Roy Thomas, senior ophthalmic surgeon to the Swansea General and Eye Hospital (in succession to Dr. J. Lloyd Davies); Mr. J. T. Morrison, dean of the faculty of medicine, University of Liverpool (in succession to Prof. T. B. Davie). Mr. Morrison is also a member of the Liverpool Regional Hospital Board.

Nuffield Medical Fellowships

For the past few years the Nuffield Foundation has offered fellowships in child health, industrial health, social medicine, and psychiatry to those who wish to qualify for an academic career as teachers and research-workers. In all there have been 121 applications and 18 fellowships have been awarded. At their meeting in June the trustees decided that the time had come to widen the scope of the scheme to include all fields of medicine while still giving special consideration to applications for additional training in the four original subjects. Further particulars will be found in our advertisement columns.

Medical Protection Society

Dr. A. R. French has been appointed secretary to the society in succession to Dr. R. W. Durand, who has resigned to take up the post of superintendent of Belfast City Hospital.

Dr. French was educated at Epsom College and the London Hospital. After taking the Conjoint qualification in 1927 he spent some time in general practice before taking a short-service commission in the medical branch of the Royal Air Force. He then went back into general practice in Greenford until he was called up in September, 1939. He served throughout the war and was for some time the officer in charge of the R.A.F. medical statistical office. After his release he studied industrial medicine and took the D.I.H. last year. He has been honorary secretary of the local division and of the Metropolitan Counties branch of the British Medical Association. He is also a member of the Medico-Legal Society, and he has served with the Pensions Appeal Tribunals.

Royal College of Obstetricians and Gynæcologists

The Dowager Lady Reading, at the annual dinner of the Royal College of Obstetricians on Oct. 1, paid great tribute to those who specialise in midwifery and the diseases of women. There are moments, she suggested, when they appear as demi-gods. In responding, Sir William Gilliatt, the president, told how the list of candidates for membership of the college has grown, from 84 in 1938 to 294 in 1948; and reminded his hearers how the college itself, presented sixteen years ago by Sir William Blair-Bell, had seemed grandiose then, but was now too small for the growing body using it. He referred to the help given by the college in reserving appointments for Dominion postgraduates who come to Great Britain for experience. Last year appointments were reserved for 6 nominated Dominion postgraduates, and additional appointments were found for 9 others who came unexpectedly.

Dr. Emil Novak, president of the American Gynecological Society, replying to Mr. V. B. Green-Armytage who proposed The Guests, was pleasant about any language difficulty which his hearers might experience; indeed, he said, there had been a language difficulty in his own family, for his wife came from Boston, and his son spoke a hybrid tongue. He had that afternoon been made an honorary fellow of the college, to which he brought a gift from the American Gynecological Society—a gavel, made from two door-knobs and a part of a newel-post taken from the house of Ephraim McDowell, the father of ovariotomy. In accepting the gavel on behalf of the college, the president remarked that another fifty years had passed before Spencer Wells did his first ovariotomy in England—though he had subsequently made up for lost time.

Sir Henry Dale, F.R.S., newborn president of the Royal Society of Medicine, claimed leave to suffer from eloquence, the occupational disease of presidents, and described how ergot, and the studies he made of it, had brought him into touch with all sorts of eager minds and famous men; and Prof. Newell W. Philpott, of McGill University, spoke kindly of the help the college had given its friends the Canadian obstetricians and gynæcologists in organising their affairs. He begged for more visits from British gynæcologists.

Middlesex Hospital Medical School

Presiding over a gathering of some 300 people at the annual dinner held in London on Oct. 1, Mr. Maurice Whiting spoke of some of his teachers—John Murray, Sir Gordon Gordon-Taylor, William Lang, and Sir Robert Young. When he entered the hospital in 1907 he was told that patients liked to go to Middlesex because they were treated with care and consideration as well as skill. Such a tradition was worth maintaining. The present position of the medical school was, he felt, largely due to the work of three of its deans, Campbell Thomson, Lord Webb-Johnson, and Dr. Boldero, all of whom had done so much in their several ways. Of a hospital it might be said that the ship was more than the crew, but the ship and crew were one. He hoped that when the Middlesex ship made its voyage into new and uncharted seas the crew would preserve its reputation. Dr. H. E. A. Boldero drew attention to the presence of Prof. Lillian Penson, the first woman vice-chancellor of the University of London and the first woman to attend the Middlesex Hospital dinner. Under the N.H.S. Act, he said, three hospitals had been added to the Middlesex—the Woodside Hospital for Functional Nervous Diseases; the British Red Cross Society's Clinic for Rheumatism, Peto Place (now renamed the Arthur Stanley institute of the Middlesex Hospital); and the Hospital for Women in Soho. He welcomed these hospitals and the great opportunities they brought. Though the medical school now had its separate charter it would remain as closely in touch as before, especially as Colonel J. J. Astor was chairman both of the hospital and of the medical school council. Dr. R. S. C. Couch, as senior Broderip scholar, spoke regretfully of the recent call-up arrangements which would deprive many of his contemporaries of the chance of holding a B2 hospital appointment. Turning to rather lighter topics, he described the invasion of the medical school by women students and seemed to think it might advantageously be carried further. Mr. E. W. Riches concluded the speeches by expressing some of the admiration and affection in which the chairman is held by his colleagues and former students.

Digitized by Google

Society of Medical Officers of Health

At a meeting of the society to be held on Thursday, Oct. 14, at B.M.A. House, Tavistock Square, W.C.1, at 5.40 P.M., Prof. R. H. Parry will be installed as president and will deliver his presidential address.

Royal London Homœopathic Hospital

The King, who is patron of the London Homœopathic Hospital, has commanded that in future it shall be known as the Royal London Homœopathic Hospital. The hospital will celebrate its centenary next year.

St. John's Hospital Dermatological Society

Dr. J. M. H. MacLeod will deliver the Prosser White oration at 1, Wimpole Street, London, W.1, on Thursday, Oct. 28, at 4.30 P.M. The title of his address is Milestones on a Dermatological Journey. A dinner will be held the same evening. Further particulars may be had from the secretary of the society, St. John's Hospital, 5, Lisle Street, W.C.2.

Royal Institute of Philosophy

In the Michælmas term a course of lectures on Foundations of the Moral Life will be given at the institute, 14, Gordon Square, London, W.C.1, on Fridays at 5.15 P.M., beginning on Oct. 15. Cards of admission may be had from the director of studies at the institute. Viscount Samuel will deliver his presidential address at 5.30 P.M. on Oct. 20. He is to speak on the Decline or Revival of Religion.

British Association of Plastic Surgeons

The clinical congress held by the association, under the presidency of Prof. T. P. Kilner, at Oxford and Stoke Mandeville from Sept. 16 to 18 was attended by 91 plastic surgeons, including visitors from America, Sweden, Norway, Belgium, Ireland, Denmark, and South America. The guest of honour was Dr. Sumner L. Koch, of Chicago, who gave an address on Surgery of the Hand.

Proper Use of the Health Service

Mr. Aneurin Bevan, Minister of Health, addressing the British Hospitals Contributory Schemes Association on Oct 1, said that the National Health Service would fail unless the people used it intelligently, sparingly, and prudently. As reported in the *Times*, he added: "There is as much need for prudence on the part of the profession in giving the benefits of the service as there is for the population in the claiming of those benefits."

King's College Hospital Medical School

The annual dinner was held in London on Oct. 2, after the formal opening of the medical school on the previous day. Prof. Henry Cohen, who had delivered the oration at the opening ceremony, was the guest of honour, and emphasised that though the increasing number of committees these days was a heavy burden to bear it was important that the responsibility should be accepted, for that was the only means whereby medical men might influence their future. Mr. Harold Edwards, the dean, pointed out that the changing needs of today necessitated considerable modification of the curriculum. Among other guests who attended were the non-medical members of the recently constituted council of the medical school, including the Marquis of Normanby, the new chairman of the hospital.

Award for Gallantry

The King has awarded the Albert Medal to Dr. A. R. C. Butson, a member of the Falkland Islands Dependencies Survey, in recognition of his gallantry in the following circumstances:

On the evening of July 26, 1947, an American member of the Ronne Antarctic Research Expedition fell into a crevasse some 6 miles from base. Two teams were sent to the rescue, but the hazards of crossing a heavily crevassed glacier were much increased by darkness, and it was not until 4 o'clock on the morning of July 27 that the crevasse into which the American had fallen was located. Butson immediately volunteered to be lowered into the crevasse where he found the American tightly wedged 106 ft. down and suffering from shock and exhaustion. For nearly an hour he had to chip the ice away in an extremely confined space in order to free the American, who was brought to the surface and placed inside a tent. Butson then rendered the necessary medical aid and at dawn a return to base was made carrying the American on one of the sledges.

Dr. Butson, who is a Cambridge graduate, qualified from University College Hospital in 1945.

Appointments

DONOVAN, G. E., M.D., M.SC. N.U.I., D.P.H.: divisional M.O., West Glamorgan.
DURAND, R. W., M.R.C.S.: superintendent, Belfast City Hospital.
HOLME, THOMAS, M.B. Manc., D.P.H.: divisional M.O.H., Stalybridge and Dukinfield, Cheshire.
TAYLOR, G. H., M.D. Lond., D.P.H.: deputy county M.O.H. and deputy school M.O., Warwickshire.

Fulham Hospital:
COMERFORD, R. E. W. B., M.A., M.B. Camb., D.A.: senior resident anæsthetist.
MCSWEENEY, TERENCE, M.B. N.U.I.: casualty officer.
WALLACE, D. M., O.B.E., M.S. Lond., F.R.C.S.: part-time registrar to genito-urinary department.

University of Wales:
Asst. M.O. for student welfare:
GRANT, GRAHAM, M.B. Lond.
WILLIAMS, LILIAS, M.B. Edin., D.P.H.

Diary of the Week

OCT. 10 TO 16

Monday, 11th

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Mr. F. S. Cooksey: Rehabilitation and Surgery.
MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8 P.M. Annual general meeting.
8.30 P.M. Dr. T. Jenner Hoskin: Thyrotoxicosis. (Presidential address.)

Tuesday, 12th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. Desmond Curran: Prefrontal Leucotomy. (First Croonian lecture.)
ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. R. C. Brock: Surgery of the Heart and Great Vessels.
INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histology of the Skin.
CHELSEA CLINICAL SOCIETY
7.30 P.M. (South Kensington Hotel, 47, Queen's Gate Terrace S.W.7.) Dr. Geoffrey Evans: Empiricism in Medicine.

Wednesday, 13th

ROYAL COLLEGE OF SURGEONS
5 P.M. Prof. J. R. Learmonth: Pathological Physiology of Peripheral Arterial Disease.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. W. G. Wyllie: Weaning and Mixed Feeding of the Infant.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
10 A.M. Mr. J. D. McLaggan: Treatment of Cardiospasm.
UNIVERSITY OF GLASGOW
8 P.M. (Department of Ophthalmology.) Dr. Paul Bacsich: Experimental Corneal Grafting.

Thursday, 14th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. Curran: Prefrontal Leucotomy. (Last Croonian lecture.)
ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. Denis Browne: Surgery of Congenital Deformities of the Extremities.
BRITISH INSTITUTE OF RADIOLOGY, 32, Welbeck Street, W.1
8 P.M. Sir Stanford Cade, Dr. J. L. Dobbie, Mr. W. D. Harmer: Carcinoma of the Buccal Cavity.
INSTITUTE OF DERMATOLOGY
5 P.M. Dr. H. J. Wallace: Erythematosquamous Eruptions.
SOCIALIST MEDICAL ASSOCIATION
7.30 P.M. *North West Middlesex Branch.* (Town Hall, Wembley.) Dr. E. H. Capel: An Industrial Health Service.

Friday, 15th

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. T. Holmes Sellors: Surgery of Pulmonary Tuberculosis.
FACULTY OF RADIOLOGISTS
2.15 P.M. *Therapy Section.* (Royal College of Surgeons.) Mr. A. J. Durden Smith, Dr. J. R. Nuttall, Mr. G. W. Blomfield: Palliative Treatment in Advanced Breast Cancer.

Mr. Aneurin Bevan, the Minister of Health, has appointed Mr. J. E. Beddoe to be his principal private secretary.

On Oct. 15 Dr. J. F. Brailsford will reach New York to begin a lecture tour in the United States during which he will address the Annual Meeting of Radiologists at San Francisco.

CORRIGENDA. — *Exchange Transfusion in Hæmolytic Disease of the Newborn* (Oct. 2, p. 522). Dr. Mollison's co-author is Miss Marie Cutbush, B.SC.

In our note last week on Dr. J. V. Dacie's appointment as reader in hæmatology at the Postgraduate Medical School of London, the word *hæmostatic* should have been *hæmolytic*.

Digitized by Google

OCT. 16, 1948 PAGES 595 TO 634

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6529 LONDON: SATURDAY, OCTOBER 16, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Streptomycin Therapy of Tuberculous Meningitis in Children
Prof. K. CHOREMIS, M.D.
N. ZERVOS, M.D.
V. CONSTANTINIDES, M.D.
S. PANTAZIS, M.D. 595

Recurrent Dislocation of the Shoulder
J. E. RICHARDSON, F.R.C.S... 599

Effect of Caronamide on Blood-penicillin Concentrations in Man
R. B. HUNTER, M.R.C.P.E.
W. M. WILSON, M.R.C.P.E.
JAMES DICK 601

Mass Deaths of Infants
THILO BREHME, DR.MED. ... 604

p-Aminobenzoic Acid in Leukæmia
H. B. MAY, M.R.C.P.
J. VALLANCE-OWEN, M.R.C.P. 607

Despeciated Bovine Serum
DAVID ANNIS, F.R.C.S..... 609

p-Aminosalicylic Acid Determination in Blood and Cerebrospinal Fluid
W. KLYNE, PH.D.
J. P. NEWHOUSE, B.SC..... 611

SPECIAL ARTICLES

Condition of Children in Western Germany
A. P. MEIKLEJOHN, B.M..... 619

Medical Research in Africa..... 624

W.H.O. Conference on Streptomycin..... 626

NEW INVENTIONS

A Spinal Needle
R. R. MACINTOSH, F.R.C.S... 612

LEADING ARTICLES

FIRST QUARTER 613

NEWS ABOUT VIRUSES..... 614

LYMPHOCYTES AND THE ADRENAL CORTEX 615

ANNOTATIONS

Medical Research Council..... 616

Nuffield Foundation 616

Medical Films..... 617

The Names of Bacteria..... 617

Aureomycin 618

Hospital Admissions in the New Service..... 618

House Committees..... 618

LETTERS TO THE EDITOR

Unfortunate Names of Hospitals 628

Infertility due to Mechanical Failure of Ovulation (Dr. Allan Palmer) 628

Independence in Research (Prof. F. W. Twort, M.R.C.S., F.R.S.).. 629

M.R.C.P. Examination 629

Assessment of Diphtheria Prophylaxis (Prof. E. Carlinfanti, M.D.) 629

Hospital Admissions and Records (Mr. B. Benjamin, B.SC.)..... 630

A Simplified Rothera's Test (Dr. G. A. Smart, Mr. G. H. Darling, PH.C.) 630

Dietary Fat (Dr. Nevil Leyton).. 630

Under Tension (Dr. P. D. H. Chapman) 631

Index for Film Records (Dr. Peter Hansell) 631

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 627

REVIEWS OF BOOKS

Fungus Diseases of the Lungs. Prof. D. T. Smith, M.D..... 611

Symposium on the Use of Isotopes in Biology and Medicine..... 611

Vitamine und Vitaminetherapie. Prof. Emil Abderhalden, Prof. Georges Mouriquand 611

Lehrbuch der inneren Sekretion. Prof. F. Verzár..... 612

Science in Progress. G. A. Baitsell 612

Bergey's Manual of Determinative Bacteriology. R. S. Breed and others..... 612

Investigations on Agonal Acidosis. I. F. Hansen..... 612

OBITUARY

George Trench Western..... 631

NOTES AND NEWS

Medical Recruits 632

The Team Spirit in Hospital..... 632

Pharmacological Relationships .. 632

University of London 633

University of Leeds..... 633

Royal College of Physicians of London 633

Royal Society of Medicine..... 633

Westminster Hospital and Medical School 633

Northern Ireland Health Service. 633

National Marriage Guidance Council..... 633

Scottish Society of the History of Medicine 633

King Edward VII's Hospital for Officers..... 633

S.M.A. on Health Centres..... 634

Minister on Health Service..... 634

Diary of the Week..... 632

Births, Marriages, and Deaths... 634

MAJOR ENDOCRINE DISORDERS

by S. LEONARD SIMPSON, *M.A., M.D. (Cantab.), F.R.C.P. (London)*

Physician, Willesden General Hospital, with charge of Diabetic and Endocrine Clinics; Endocrinologist, Princess Louise Children's Unit of St. Mary's Hospital; Consulting Physician and Endocrinologist, Soho and Samaritan Hospitals for Women

"Well written, well illustrated, very readable account of an interesting subject."
—CLINICAL JOURNAL

SECOND EDITION 574 pages 122 illustrations 42s. net

OXFORD UNIVERSITY PRESS

Digitized by Google

OXFORD MEDICAL PUBLICATIONS

POST-MORTEM APPEARANCES

by JOAN M. ROSS, *M.D., B.S., M.R.C.S., L.R.C.P.* FIFTH EDITION 318 *pages* 8*s.* 6*d. net*

PHARMACOLOGY

by J. H. GADDUM, *Sc.D., F.R.S., M.R.C.S., L.R.C.P.* THIRD EDITION 520 *pages* 79 *illustrations* 17 *tables* 25*s. net*

CHANGING DISCIPLINES

by J. A. RYLE, *M.D., F.R.C.P.* 140 *pages* 13 *illustrations* 10 *tables* 12*s.* 6*d. net*

MANAGEMENT IN OBSTETRICS

by A. M. CLAYE, *M.D., F.R.C.S., F.R.C.O.G.* 196 *pages* 17 *illustrations* 12*s.* 6*d. net*

BREAST FEEDING

by F. CHARLOTTE NAISH, *B.A., M.D.* (*Sir Charles Hastings Clinical Essay Prize*, 1947). *With a Foreword by* ALAN MONCRIEFF, *M.D., F.R.C.P.* 164 *pages* 20 *illustrations* 10 *tables* 10*s.* 6*d. net*

THE BACKGROUND OF THERAPEUTICS

by J. HAROLD BURN, *M.D., F.R.S.* 376 *pages* 59 *illustrations* 26 *tables* 22*s.* 6*d. net*

PSYCHOTHERAPY: ITS USES AND LIMITATIONS

by D. R. ALLISON, *M.D., M.R.C.P., and* R. G. GORDON, *M.D., D.Sc., F.R.C.P.* 168 *pages* 8*s.* 6*d. net*

THE PARATHYROID GLANDS AND SKELETON IN RENAL DISEASE

by J. R. GILMOUR, *M.R.C.P.* 172 *pages* 26 *illustrations* 18*s. net*

OBSTETRICS AND GYNÆCOLOGY

by C. SCOTT RUSSELL, *M.B., F.R.C.S., M.R.C.O.G. With a Foreword by* J. CHASSAR MOIR, *D.M., F.R.C.S., F.R.C.O.G.* 222 *pages* 21 *illustrations* 12*s.* 6*d. net*

PRACTICAL TEXTBOOK OF LEPROSY

by R. G. COCHRANE, *M.D., F.R.C.P., D.T.M. & H. With a Foreword by* Sir GEORGE McROBERT, *C.I.E., M.D., F.R.C.P., D.T.M. & H.* 296 *pages* 175 *illustrations* 42*s. net*

DISEASES OF THE NERVOUS SYSTEM

by W. RUSSELL BRAIN, *D.M., F.R.C.P.* THIRD EDITION 1008 *pages.* 79 *illustrations* 37*s.* 6*d. net*

SENSORY MECHANISMS OF THE RETINA

by RAGNAR GRANIT, *M.D.* 432 *pages* 178 *illustrations* 35*s. net*

OXFORD UNIVERSITY PRESS

Digitized by Google

STREPTOMYCIN THERAPY OF TUBERCULOUS MENINGITIS IN CHILDREN

K. CHOREMIS
M.D. Athens
PROFESSOR OF PÆDIATRICS AND DIRECTOR OF PÆDIATRIC CLINIC, UNIVERSITY OF ATHENS

N. ZERVOS
M.D. Pisa
ASSOCIATE PROFESSOR OF PÆDIATRICS TO THE CLINIC

V. CONSTANTINIDES
M.D. Athens
SENIOR ASSISTANT PHYSICIAN

S. PANTAZIS
M.D. Athens
CHIEF OF BACTERIOLOGY DIVISION OF THE CLINIC

FROM April 1 to Nov. 30, 1947, 72 cases of tuberculous meningitis were treated in the Pædiatric Clinic of the University of Athens. Of these cases 13 began as miliary tuberculosis and 59 as a severe primary infection with, in some cases, a perifocal spread. Thoracic spondylitis was present in 3 cases, and 1 case was a sequel to cervical adenitis.

In 9 cases no streptomycin was given and death ensued. Streptomycin was given to the remaining 63 patients (tables I and II). Combined intramuscular and intrathecal therapy was applied routinely, and intrathecal therapy was regarded as indispensable. Of these 63 patients, 34 died and 29 survived. In almost all our fatal cases necropsy was refused.

Enough patients have survived for a sufficient period to allow us to observe phases of tuberculous meningitis which in pre-streptomycin days were very brief or, in most cases, never seen. We feel that the full potentialities of streptomycin will not be disclosed until the dosage, method of administration, and duration of treatment are correlated with the clinical and biological progress of the disease.

Four factors must be considered together in planning the attack with streptomycin and in managing the course of treatment: the antibacterial power of streptomycin; the acquired resistance of *Myco. tuberculosis* to streptomycin; the toxic effects of streptomycin; and the stage of the disease at which treatment is begun. Our investigations have been directed towards elucidating the relationship between the third and fourth factors and the progress of the tuberculosis, for here, we believe, lies the secret of the best use of streptomycin.

We are not impressed with the significance of the presence of *Myco. tuberculosis* in the cerebrospinal fluid (C.S.F.). We have evidence, both from our own experience and from that of others, that the finding of this bacillus in the C.S.F. is not inevitably followed by tuberculous meningitis. We lately reported [1] cases of meningism, with *Myco. tuberculosis* in the C.S.F., associated with primary tuberculosis in children, where no meningitis developed and with no specific treatment the children recovered in a few days. We have also recently discharged patients who have had tuberculous meningitis treated with streptomycin and whose clinical condition and C.S.F. findings have become normal except for the continued presence of *Myco. tuberculosis* in the C.S.F. After varying periods there has been no relapse in these cases and certainly there has been no immediate recurrence of the meningitis.

DOSAGE

Opinions vary considerably about the dosage of streptomycin in tuberculous meningitis. At first we gave 2 g. of streptomycin daily, but later we reduced the dose to 1 g. daily or even less. The optimum dosage depends on the patient's age and on the stage of the disease. Both intramuscular and intrathecal administration were used (tables I and II), and we are now satisfied that the more severe the signs the smaller should be the intrathecal dose. Thus, to an infant with advanced tuberculosis we would give 0·5–0·6 g. daily, of which 0·05 g. would be intrathecal and the rest intramuscular. The intrathecal dose may even be less than 0·05 g. —sometimes as little as 0·01 g.

DURATION OF TREATMENT

Here again there is great difficulty, but in our experience three or four months is the average period during which streptomycin will exert its main therapeutic effect. We combine continuous and intermittent administration to put off for as long as possible the acquisition of tolerance of streptomycin by the bacillus and to avoid the unwelcome effects of protracted intrathecal injection.

In general we give about four to six weeks' initial treatment, both intrathecally and intramuscularly. We usually find a well-marked amelioration of signs and symptoms at the end of this, but laboratory reports show that tuberculosis is still present. We call this the *period of clinical improvement.*

We next discontinue treatment for five to ten days, after which we resume treatment for ten to fifteen days. There follows a further rest period and then further treatment as before, and this phase of intermittent treatment may go on for as long as three months. Our treatment in this phase depends on the laboratory findings, for as a rule the patients by now show no evidence of meningitis. We call this stage the *stage of laboratory restitution.*

We agree with other observers that, after the first and acute stage is over, the patient's clinical appearance is no indication for stopping treatment. Further, while the cell-count and biochemical findings show that the C.S.F. is still abnormal, the probability, perhaps even certainty, is that the child will have an exacerbation. Therefore, while the C.S.F. findings show any signs of tuberculous meningitis the treatment must go on.

METHODS OF ADMINISTRATION

It is known that streptomycin has a local effect. We have seen immediate regression in cases of adenitis and fistulæ under local streptomycin therapy. Nevertheless, some workers have queried the desirability of intrathecal administration and have used only the intramuscular route. The irritant effects of streptomycin on the theca have been confirmed by our experience. Intrathecal streptomycin leads to an increase in the amount, the cell-count, and the albumin content of the C.S.F., and a long series of intrathecal injections may cause complete obstruction of the spinal canal.

Advanced tuberculous meningitis always produces an acute hydrocephalus, and the paralytic stage follows. Therefore, in view of the known tendency of intrathecal streptomycin to irritate and bring about blockage of the cerebrospinal canal, the risk of aggravating a natural tendency of the meningitis should be kept in mind. At the start of our experiments, when large doses (0.1 g. or more) were given, we have seen an aggravation of meningitis, including hydrocephalus, under the influence of intrathecal streptomycin, and death has been accelerated in this way.

Yet we believe, with others, that intrathecal therapy is indispensable in the treatment of tuberculous meningitis. We tested the intrathecal action of streptomycin on three physically healthy children, with the results shown in table III. In other cases we have noted that continuous intrathecal injection leads to blockage of the flow of C.S.F. to the point of occlusion and dry puncture. We can only regard this as the result of injury to, and irritation of, the meninges; in fact a necropsy showed a local traumatic adhesive meningitis completely interrupting the flow of C.S.F. Since we began intermittent treatment we have not observed any blockage at all.

1. Choremis, K., Vrachnos, G. *Lancet*, Sept. 11, p. 408.

Digitized by Google

Streptomycin modifies the classical picture of tuberculous meningitis in its two stages, inflammatory and hydrocephalic, and by prolonging the patient's life increases the incidence of extreme hydrocephalus with fontanelles and even cranial sutures widely open. It is a weakness of the treatment that streptomycin contributes to this effect both directly and indirectly by lengthening the disease. In our earlier cases our persistence with large intrathecal doses undoubtedly contributed to a fatal issue.

We no longer see deaths in the paralytic state as we did before the introduction of streptomycin, but there are many more deaths from acute hydrocephalus. The signs which should be carefully watched for in streptomycin treatment are gradually increasing opisthotonos, repeated uncontrollable vomiting, a sudden increase in pulse-rate,

TABLE I—EFFECTIVE TREATMENT WITH STREPTOMYCIN

Case no.	Age	Date of admission (1947)	Date of discharge	Weight (kg.)	Dosage (g.)			*Myco. tuberculosis* in C.S.F.	Fundus examination for tubercles	Months from cessation of treatment to March 31, 1948	Remarks
					I.M.	I.T.	Total per kg. body weight				
TUBERCULOUS MENINGITIS											
Cured according to clinical and laboratory findings:											
1	2½ yr.	May 12	Aug. 19, 1947	15	37·6	2·0	2·6	+	+	8	No disturbance of hearing or of vestibular function
2	6 ,,	May 29	Nov. 12, ,,	20	50·4	5·7	2·8	+	+	5	Temporary mental confusion, now clear
3	13 ,,	April 6	June 26, ,,	35	55·2	4·1	1·6	..	..	9½	No disturbance of hearing or of vestibular function
4	2 ,,	June 1	Oct. 16, ,,	13	88·4	5·7	7·2	..	+	6	,,
5	13 ,,	April 4	July 14, ,,	40	66·0	4·0	1·75	..	..	9	,,
6	5 ,,	May 30	Aug. 16, ,,	15	51·2	3·4	3·6	..	+	8	,,
7	6½ ,,	Aug. 15	Nov. 26, ,,	7	29·0	1·45	4·4	+	+	5	,,
8	2½ ,,	April 1	Oct. 6, ,,	11	52·8	3·35	5·0	+	..	6	,,
9	7 ,,	April 3	July 2, ,,	22	66·0	7·7	3·32	..	+	9	,,
10	15 mos.	May 22	Dec. 9, ,,	7·5	55·35	7·0	8·4	+	..	4	Permanent disturbance of 8th nerve
11	14 yr.	Aug. 15	Dec. 4, ,,	31	75·4	3·25	2·5	+	..	4	No disturbance of hearing or of vestibular function
12	6 ,,	June 20	Dec. 21, ,,	20	95·0	5·0	5·0	+	..	4	,,
13	8 ,,	May 5	Dec. 11, ,,	23	75·5	7·5	3·6	..	..	4	,,
14	10 ,,	April 6	Dec. 16, ,,	40	113·0	7·0	3·0	+	+	4	,,
15	3½ ,,	July 7	March 9, 1948	12	82·4	3·75	7·0	..	..	4	,,
16	11 ,,	Aug. 3	Jan. 15, ,,	30	68·0	4·2	2·4	+	+	3	,,
17	4 mos.	Aug. 7	Jan. 15, ,,	4	45·0	3·0	12·0	+	..	3	,,
18	11 yr.	July 24	Feb. 24, ,,	31	93·0	7·0	3·2	+	+	2	,,
19	9 ,,	Oct. 4	March 6, ,,	30	55·7	2·3	1·93	+	..	1½	,,
20	9 ,,	Oct. 4	March 9, ,,	27	54·3	3·2	2·1	+	..	1½	,,
21	11 ,,	Nov. 23	March 10, ,,	28	34·2	2·8	1·3	+	..	1¼	,,
Cured clinically but not according to laboratory findings:											
22	14 yr.	Oct. 24	Still in hospital	52	48·7	7·3	1·08	+	..	..	..
23	11½ ,,	Oct. 31	,,	50	47·6	2·4	1·0	+	..	1¼	..
24	20 mos.	Nov. 26	,,	10	19·9	1·5	2·1	+	..	..	..
MILIARY TUBERCULOSIS WITH TUBERCULOUS MENINGITIS											
25	8 yr.	April 11	Oct. 5, 1947	22	51·2	4·5	2·5	*+	+	6	Cured according to clinical and laboratory findings; no relapse
26	2 ,,	April 6	July 5, ,,	12	25·6	1·4	2·25	+	..	9	Cured according to clinical and laboratory findings on discharge, but relapsed on March 6, 1948
27	2 ,,	Sept. 15	Still in hospital	8	61·5	1·5	7·87	+	..	..	Clinically improved
28	2½ ,,	July 25	Jan. 19, 1948	11·7	94·4	2·1	8·2	..	..	3	Cured according to clinical and laboratory findings, but relapsed on March 8, 1948
29	11 ,,	July 30	Jan. 25, ,,	24	39·8	0·8	1·75	+	..	3	Cured according to clinical and laboratory findings; no relapse

* Tuberculous spondylitis.

Digitized by Google

and respiratory disturbances going on perhaps to Cheyne-Stokes breathing; the persistence of any of these is an indication for the absolute cessation of streptomycin therapy; cisternal puncture is the only useful palliative measure. If the signs improve, small daily intrathecal doses (beginning, say, with 0·01 g.) may be started again and slowly increased, so long as none of the above signs and symptoms recurs. It may be necessary to keep the dose minimal for many days, but we have observed that, when the crisis has safely passed, the intrathecal dose can be increased from 0·01 to 0·1 g.

Large Intrathecal Daily Doses in Early Cases.—The more advanced the meningitis the greater the reaction to intrathecal streptomycin, and a patient admitted with no irritative symptoms can tolerate relatively larger doses. The rationale of large early intrathecal doses is to combat the bacilli when the symptoms and signs are relatively slight and the meningeal irritation is not well marked, with no evidence of hydrocephalus or paralytic phenomena. As the clinical picture improves, the doses may be decreased gradually until they can be abandoned in favour of intramuscular therapy alone. There is a very definite risk that intrathecal streptomycin will aid the production of hydrocephalus. In early cases this risk must be taken, but the nearer one gets to the hydrocephalic stage the more care is necessary with intrathecal therapy.

RESULTS

Tuberculous Meningitis

Of the 50 patients treated 21 have been discharged cured according to clinical and laboratory findings, 3 are still under treatment and show clinical improvement but with significant laboratory findings, and 26 have died (tables I and II).

In most of the 21 cases cured, treatment was begun in the first ten days of disease. Two broad phases can be described: (1) clinical improvement; and (2) recovery confirmed by C.S.F. laboratory findings. During clinical improvement intensive intrathecal and intramuscular treatment was given with the immediate aim of arresting the disease, and relatively large doses were administered. This phase lasted, on an average, four or five weeks, and by that time the clinical picture had become normal and we gave a favourable prognosis. The phase of recovery averaged two or three months, during which we still gave both intramuscular and intrathecal streptomycin but in smaller doses, the intramuscular dose being much larger than the intrathecal, which was steadily reduced. During this phase intermittent treatment was continued until the C.S.F. had become almost normal (albumin 0·03 g. per 100 g., and cells fewer than 10 per c.mm.). The periods of "rest" were gradually lengthened. After this, further treatment for a month by the intramuscular route was given and then the patient was discharged. The patient remained under weekly observation and after three months was given ten days' intramuscular therapy, repeated at three-monthly intervals during the first year. Some of these cases have been under treatment and observation for about a year now (table I), and in none of them has any sign of relapse been seen, and they are perfectly well.

The 3 patients in whom the laboratory findings have not confirmed what appears to be a clinical cure (table I) are still under treatment.

Of the 26 patients who died (table II), 3 had received what might be called a full course of treatment—i.e., long enough for a favourable effect to show itself if it were going to appear at all—and 23 died before they had received a full course of treatment. In every one of this group the history suggests that the disease had lasted at least fifteen days before the child was given intrathecal streptomycin. Table II shows that streptomycin clearly prolonged the disease in 7 cases and possibly in more,

TABLE II—INEFFECTIVE TREATMENT WITH STREPTOMYCIN

Case no.	Age	Date of admission (1947)	Weight (kg.)	Duration of treatment (days)	Dosage (g.) I.M.	Dosage (g.) I.T.	Dosage (g.) Total per kg. body-weight	*Myco. tuberculosis*
TUBERCULOUS MENINGITIS								
Regular treatment:								
30	3 yr.	June 25	12	80	60·4	1·8	5·0	+
31	14 mos.	Sept. 12	8·5	38	31·8	1·65	4·0	+
Incomplete treatment:								
32	3 yr.	May 31	11	39	28·4	3·7	2·9	..
33	6 ,,	Oct. 3	18	13	22·8	1·3	1·3	+
34	13½ mos.	Sept. 30	9	15	2·4	0·3	0·3	+
35	4 yr.	Sept. 16	13	3	3·6	0·35	0·3	+
36	10 ,,	Sept. 27	27	5	3·2	0·4	0·13	+
37	4 ,,	Aug. 12	12·5	3	2·6	0·3	0·24	..
38	2 ,,	July 22	10·5	9	5·0	0·5	0·55	..
39	22 mos.	Oct. 31	9	28	17·75	0·25	2·0	+
40	10 yr.	March 24	28	25	1·8	0·2	0·07	+
41	5 ,,	April 4	14	18	5·9	0·6	0·46	..
42	12 ,,	May 26	33	1	0·8	0·2	0·03	..
43	2½ ,,	June 5	12	6	4·3	0·7	0·4	+
44	10 ,,	June 13	26	2	1·4	0·1	0·058	+
45	18 mos.	June 18	9·5	2	1·8	0·2	0·22	..
46	3 yr.	July 23	12·5	2	1·8	0·2	0·16	..
47	10 ,,	July 28	28	7	5·5	0·5	0·22	..
48	4 ,,	Aug. 19	13·5	2	0·4	0·1	0·04	..
49	3 ,,	Sept. 4	12	2	1·45	0·05	0·13	+
50	21 mos.	Nov. 5	8·5	4	2·56	0·14	0·32	+
51	14 ,,	Oct. 25	10	2	2·4	0·1	0·25	+
52	3 yr.	Nov. 15	12	2	0·95	0·05	0·08	+
53	7 ,,	Nov. 25	20	22	17·9	0·37	0·91	..
54	22 mos.	Nov. 22	10	7	6·0	0·04	0·6	..
55	2 yr.	Nov. 20	10·5	16	6·6	0·4	0·66	..
MILIARY TUBERCULOSIS WITH TUBERCULOUS MENINGITIS								
Complete treatment:								
56	11 yr.	May 12	25	123	80·7	4·0	3·4	+
57	9½ mos.	July 23	5	103	43·8	0·25	8·8	+
58	15 yr.	Nov. 15	38	40	68·0	2·0	1·8	+
Incomplete treatment:								
59	11 mos.	June 11	7	8	8·0	0·5	1·2	+
60	12 ,,	Oct. 10	9	15	6·0	0·7	0·7	+
61	20 ,,	Oct. 13	8·5	4	2·8	0·2	0·36	..
62	6 ,,	Nov. 3	5·5	3	1·0	0·2	0·22	+
63	5½ yr.	Oct. 2	15	18	4·8	0·5	0·36	+

Note relatively few deaths in those who survived more than a few days.
"Complete" treatment refers to cases which had a substantial amount of streptomycin which in other cases has produced a cure, whereas those given "incomplete" treatment died before a possibly curative dosage could be completed.

and its clinical course was changed from that which we have seen so many hundreds of times in pre-streptomycin days.

Some 14 of these children died within a week of admission to hospital. Among them the signs of hydrocephalus were slight and the rise of tension of the C.S.F. was not well marked. No true opisthotonos developed. In the final stages the temperature and pulse-rate rose suddenly, the temperature rising higher and more quickly than the pulse-rate, so that the pulse line crossed the temperature line on the chart, a phenomenon often noted by Continental workers.

On the other hand, where treatment had been lengthy, death was a direct result of excessive intracerebral tension due to acute hydrocephalus. The evolution of tuberculous meningitis to this stage is undoubtedly due to the prolongation of the disease by streptomycin.

We cannot explain the failure of streptomycin in this group, but delay in starting treatment certainly limits its favourable effects and makes administration more hazardous. For reasons mentioned above, intrathecal streptomycin given at the wrong time, in advanced stages of tuberculous meningitis, may accelerate the end and possibly be the actual cause of death.

A few of the children had been treated before admission with intramuscular streptomycin for three weeks or more. None of these recovered, and we believe that intramuscular streptomycin does nothing towards preventing

Digitized by Google

TABLE III—EFFECTS OF INTRATHECAL INJECTIONS OF STEPTOMYCIN IN HEALTHY CHILDREN

Child	Age (yr.)	Daily intrathecal dose (g.)	Cerebrospinal fluid						Remarks
			Albumin (g. per 100 ml.)		Cells (per c.mm.)		Sugar (Benedict) (mg. per 100 ml.)	Chlorides (g. per 100 ml.), as sodium chloride	
			Before injection	24 hr. after injection	Before injection	24 hr. after injection			
A	4	0·15	0·02	0·15	2–3 lymphs	1800 polys	..	..	Rise of temperature from 98·4 to 103°F after injection; convulsions and vomiting. Only one injection given
B	3½	0·05	0·025	0·04	2–4 lymphs	340 polys	40–50	0·7–1·0	These injections were continued for six days. After two more days lumbar C.S.F. contained albumin 0·035 g. per 100 ml. while cisterna fluid contained albumin 0·025 g. per 100 ml., and lumbar cell-count was 176 per c.mm. against cisternal count of 65 per c.mm. There was no change in either sugar or chlorides
C	3	0·05	0·02	0·03	3–4 lymphs	222 polys	40–50	0·7	Treatment given for six days and then stopped. Two days later lumbar C.S.F. contained albumin 0·03 g. per 100 ml. while cisternal fluid contained albumin 0·02 g. per 100 ml. and lumbar cell-count was 108 per c.mm., while cisternal count was 30 per c.mm. with 75% polymorphs. In this case, before treatment, both lumbar and cisterna punctures were done and showed the same amount of albumin and cells in each. There was no change in either sugar or chlorides in this case

hydrocephalus and the increased tension, and that when we started intrathecal treatment we probably did more harm than good.

Death took place more often among the very young than among older children. The average age of the 21 patients who recovered was 6 years 11 months, whereas that of the 26 who died was 4 years 8 months. The difficulty of early diagnosis in infants, plus the association of the meningitis with primary tuberculosis in so many cases, contributes to this. Moreover, the antigenic resistance in infants is lower than in older children. We also found miliary tuberculosis more often in the very young, and some of our patients had tuberculous bronchopneumonia.

Miliary Tuberculosis with Tuberculous Meningitis

Of 13 cases in this group (tables I and II), 2 seem to have been cured, according to clinical, radiological, and laboratory standards, some twelve months after admission; 2 were discharged with clear clinical, radiological, and laboratory findings, but have relapsed with meningitis twelve months after admission and six months after the end of treatment in the one case, and eight and a half months after admission and three months after the end of treatment in the other. One child has improved —i.e., the clinical condition is good but the laboratory findings are abnormal—and is still under treatment after six months; and the other 8 children died—3 after lengthy treatment, and 5 before a full course of streptomycin could be completed.

The relatively small number of patients with miliary tuberculosis who are either admitted with tuberculous meningitis or develop it later (in this series 13 out of 66, and in an earlier pre-streptomycin series about 10 in 100) makes us wonder what, if any, is the connexion between the two conditions. The treatment of miliary tuberculosis with streptomycin has not prevented tuberculous meningitis arising as a complication under a somewhat disguised clinical aspect. (We have never known miliary tuberculosis to follow tuberculous meningitis.) Since December, 1947, however, 8 cases of miliary tuberculosis treated with streptomycin have not shown any meningitis. We have seen so many cases of primary tuberculosis in children up to 2 years of age, with enlargement of the paratracheal glands (as opposed to the hilar group), go on directly to tuberculous meningitis that we feel that this is more than a chance happening. Of 18 children with tuberculous paratracheal adenitis in pre-streptomycin days 12 died of tuberculous meningitis within six months of the first diagnosis of glandular tuberculosis.

The development of meningitis cannot be excluded even when a case of miliary tuberculosis seems to be doing well under streptomycin. In miliary cases that develop meningitis the method of administration is the same as for uncomplicated tuberculous meningitis. The course of the disease is longer, and prognosis is difficult, with the age of the patient as an important factor. Miliary tuberculosis with tuberculous meningitis in infants is the most severe and intractable form of tuberculosis which we have submitted to streptomycin therapy. We perform regular spinal puncture in all cases of miliary tuberculosis in an effort to obtain early information about asymptomatic or camouflaged meningitis. The prognosis when a patient is admitted with both forms is bad, but it seems to be better when a patient with miliary tuberculosis develops meningitis after some treatment with streptomycin.

INFLUENCE OF STREPTOMYCIN THERAPY ON MANTOUX REACTION, E.S.R., AND C.S.F. FINDINGS

Mantoux Reaction.—We use Koch O.T. 1/10,000 on the flexor aspect of the wrist or on the inner thigh. We read the result after twenty-four hours, and measure the reaction by the method of Gröer. The test is repeated every fifteen days during treatment. In cases admitted in an advanced stage the Mantoux is negative. But as treatment goes on and improvement begins the reaction becomes positive and more strongly so as improvement continues. In cases not so severe on admission we find the reaction strongly positive during the initial phases of treatment, decreasing and remaining at a lower level, and finally rising again as the tuberculosis definitely regresses. The reaction has remained strongly positive in all children who have been discharged and report back for control. When charted according to the Gröer scheme, the reaction shows three stages: (1) the acute, with a high curve to the end of the period of clinical improvement; (2) the sustained, with a lower curve which continues until the following stage; and (3) the convalescent, or perhaps recovered, stage where the curve again becomes high. In advanced cases which are

Digitized by Google

admitted with a positive Mantoux and end fatally the positive reaction persists throughout.

Erythrocyte-sedimentation Rates (E.S.R.).—These do not help very much. They are so irregular that one cannot draw conclusions from them. The rate is often high at the start of treatment and low when much improvement has taken place.

Lipase in C.S.F.—We do not know of other investigations into the variations of the lipase content of the C.S.F., and our conclusions are submitted with reserve. We use the Comfort-Osterberg method of evaluation, and we note that the lipase content seems to be lower in advanced stages of tuberculosis during the primary phase of therapy. It becomes even lower but rises again as soon as the patient's condition has definitely improved.

Sugar and Chlorides in C.S.F.—Diminution and irregular variations of the sugar and chlorides are noted initially, but as improvement takes place their quantities increase and tend to remain within normal limits.

SECONDARY EFFECTS AND TOXICITY

We are satisfied that vertigo, headache, and vomiting are due to streptomycin, but these symptoms do not persist. We believe also that the ocular phenomena which have been described are mainly due to the tuberculosis and tend to disappear under streptomycin therapy. We wish to draw special attention to alterations in the fundus. Of the 21 patients discharged as cured a baby aged 6 months presented with a partial atrophy of the papilla, which was cured after four months' treatment. A second showed atrophy of the papilla and cerebellar disturbances. Both of these cases were given relatively large doses of streptomycin. Another case developed a well-marked hypertrichosis on the front of the leg which later regressed. One patient showed mental confusion and logorrhœa which, though diminishing, still persist. Another presented the same symptoms which cleared quickly. In 2 patients paresis of the left leg was seen, and both are improving. One case only shows permanent disturbance of the eighth nerve. We have not observed any toxic effects other than these.

AUXILIARY THERAPY

We have used tuberculin in all our cases, except those which proved fatal soon after admission. We sought to reinforce the effects of streptomycin, having been led to the conclusion that streptomycin modifies the tuberculin reaction and, we think, intensifies it. We feel too that, under streptomycin, the margin between the toxic and therapeutic doses of tuberculin becomes wider. We do not know whether the very small doses of streptomycin we use have anything to do with this, and we do no more than report the fact. We have, however, divided a later series of cases and are treating half of them with streptomycin and tuberculin and half without tuberculin.

We have in certain cases, where the general condition was very poor, given blood-transfusions with temporary relief and a gain of time, and we have also given each patient concentrated vitamins A and D.

SUMMARY

Streptomycin therapy was given to 63 children with tuberculous meningitis, 13 of whom also had miliary tuberculosis.

Cures, according to both clinical and laboratory findings, can be obtained with combined intramuscular and intrathecal injections of streptomycin, recovery being accompanied by a high degree of allergy.

Early treatment with streptomycin is of prime importance—the earlier the treatment the more favourable the prognosis. By "early" is meant within the first ten days from the onset. This does not mean that the apparently hopelessly ill patient cannot be cured; nor that every early case can be cured.

In cases which do not respond to streptomycin a streptomycin-resistant strain of *Myco. tuberculosis* is probably present, but we have no laboratory confirmation of this.

Undesirable effects seem to be more the result of the disease in advanced stages than of the streptomycin in the doses we have come to use.

Dosage depends on the time when treatment is begun in relation to the stage of the disease, and to a less extent on the patient's age. Very young children usually need and tolerate streptomycin in larger doses per unit of body-weight than do older ones. Our dosage is the smallest so far recorded. Tuberculous meningitis combined with miliary tuberculosis needs larger doses and longer treatment than meningitis alone.

Our best results have been with intermittent treatment with intervals of rest.

We believe that paratracheal adenitis in primary tuberculosis is too often a forerunner of tuberculous meningitis for this to be regarded as coincidental, and we consider that streptomycin should be used in the treatment of severe cases of primary tuberculosis in children. Of 18 such patients 12 subsequently developed tuberculous meningitis.

We are unable to give an opinion on the danger of creating streptomycin-resistant strains of *Myco. tuberculosis*.

Intrathecal streptomycin is essential in tuberculous meningitis. The intrathecal dosage should be kept to the effective minimum. The effect of the drug must be watched all the time, and wrong dosage will add an unfavourable element to the progress of the disease.

We express our deep gratitude to Dr. J. M. Vine, chief of the Greece Mission of the World Health Organisation, for help in translating our observations into English and for his collaboration in the discussion of our work.

RECURRENT DISLOCATION OF THE SHOULDER

THE SURGICAL TREATMENT

J. E. RICHARDSON
M.S. Lond., F.R.C.S.
LATE SURGICAL FIRST ASSISTANT AND REGISTRAR, LONDON HOSPITAL

THE anatomical and physiological causes of recurrent dislocation of the shoulder may be summarised as a deficiency in the anterior part of the capsule, due to either stretching or rupture, with a weakness of the spinati muscles, allowing the intact subscapularis muscle to pull the head of the humerus forwards out of a normally shallow glenoid cavity. The importance of the bone lesions appears to be secondary in that they are probably the result rather than the cause of the dislocation. If, however, there is any congenital deficiency in front of the glenoid cavity or behind the humerus, this will strongly predispose the shoulder-joint to recurrent dislocations.

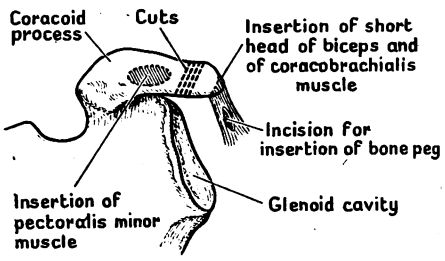
Based on these structural and functional changes, the rational treatment to prevent further dislocation is to repair the capsule, restore the muscular balance, and increase the area of the articular surfaces. In any operation, however, the possibility of producing adhesions must be considered. These adhesions can be either extra-articular or intra-articular. The extra-articular adhesions will be situated in the operation wound; since the approach is usually anterior, the adhesions will be mainly in front of the joint. Intra-articular adhesions are much more important. In any procedure in which the shoulder-joint is opened a hæmarthrosis is likely, since no tourniquet can be applied above the site of the operation, and it is impossible to apply any firm bandage to control the reactionary hæmorrhage.

Digitized by Google

It is a clinical observation that those shoulders which are rather stiff after operation are unlikely to suffer further dislocation. It seems probable that both the stiffness and the stability of the head of the humerus are due to the adhesions.

BANKART'S OPERATION

The operation most used at present is the one usually attributed to Blundell Bankart (1938), which is similar in many respects to that of Oudard (1924). The joint is approached through a straight incision in the deltopectoral groove; the coracoid process and the subscapularis muscle are then divided, and an attempt is made to repair the capsule. The practical difficulties in this step are considerable. The lesion is situated deep down in a narrow wound which easily fills with blood. The difficulties in drilling the necessary holes in the glenoid cavity and in inserting the sutures are great. Even if the torn structures are reapposed, there is considerable doubt whether they will be permanently united by the formation of fibrous tissue.



In the repair of the wound the subscapularis muscle is sutured. Muscle has a good blood-supply and unites well, provided it is kept in apposition; but, being deficient in fibrous tissue, it holds sutures poorly. During the spasms which occur when the patient is coming round from the anæsthetic the muscle must contract, throwing tension on these sutures. The sutures may tear and weaken, allowing the muscle to retract and a small gap to appear between the cut ends. The muscle is thus elongated and weakened. Thus inadvertently this operation, by reducing the power of the subscapularis muscle, may restore the normal balance between this muscle and its opponents.

The next stage in the repair of the wound is the suture of the coracoid process. The coracobrachialis muscle and the short head of the biceps muscle are attached to the distal fragment. These, by their contraction, will tend to pull this fragment downwards; again it seems likely that a gap is formed between the two fragments which subsequently becomes filled with callus and bone. The coracoid process is thus elongated and may act as a buttress in front of the head of the humerus, thus fortuitously increasing the "functional" articular area.

PRESENT OPERATION

This is based on the assumption that recurrent dislocation of the head of the humerus after Bankart's operation might in part be prevented by the elongation of the coracoid process as just described. It was hoped that a coracoid process somewhat resembling that found in patients with Erb's palsy could be created. If such a buttress could be built up it would adequately prevent further dislocation of the head of the humerus.

The coracoid process is approached through a straight incision. The deltoid and pectoral muscles are retracted. The part of the coracoid process distal to the insertion of the pectoralis minor muscle is divided by four oblique cuts with an osteotome (see figure), care being taken not to strip from the resulting pieces of bone the fibrous tissue carrying their blood-supply. The pieces of bone are then levered apart, the most distal fragment being displaced downwards and outwards. As many chip grafts as possible are forced between the pieces of coracoid process. No attempt is made to dissect the process clear, for it is from the attached soft tissues that the bone derives its blood-supply. The coracobrachialis muscle and the short head of the biceps muscle, at their insertions into the tip of the coracoid process, form a rounded muscle almost surrounded by an envelope of fibrous tissue. A vertical incision is made in this fibrous tissue (see figure) to enable a peg graft to be driven upwards into the tip of the coracoid process. The envelope of fibrous tissue is next sutured to hold the bone peg in the muscles. The wound is closed in layers. The patient's arm is kept by his side in a sling for some six weeks to allow the bone to consolidate.

RESULTS

The cases recorded in the accompanying table were all in Servicemen aged 20–40 years. In none of them was there any history of epileptic fits. The series includes all the cases admitted to hospital during this period.

On 15 patients 16 operations were performed (1 patient was subject to recurrent dislocation of both shoulders).

RESULTS OF OPERATION

Case no.	Date of last report	Side and no. of dislocations	Date of operation	Occupation	Recreation	Range of movement	Recurrences
1	May 6, 1947	Left 11	Oct. 19, 1945	Manager, ice rink	Skating	Full	None
2	May 6, 1947	Left 30–40	Nov. 19, 1945	Painter	Football and swimming	Full	None
3	May 6, 1947	Left 32	Nov. 26, 1945	Hotel manager	Squash	Full	None
4	May 7, 1947	Right 8	Dec. 17, 1945	Joiner	Football	Full	None
5	May 8, 1947	Right 4	Dec. 26, 1945	Farmer	None	Full	3
6	May 15, 1947	Left 30–40	Jan. 14, 1946	Bus conductor	Gardening	Full	None
7	May 21, 1947	Left 21	Dec. 4, 1945	Agricultural worker	Hockey	Full	None
8	May 21, 1947	Left 26	Feb. 20, 1946	Painter	Cricket	Full	None
9	June 8, 1947	Left 10	March 18, 1946	Bricklayer	Games and swimming	Full	None
10	June 20, 1947	Right 6	Dec. 19, 1945	Engine fitter	None	Full	None
11	July 15, 1947	Left 6	Feb. 18, 1946	Builder	Games	Full	None
12	March 10, 1947	Right 2 following "Nicola"	Nov. 21, 1945	Light work	None	Limited	3
13	March 20, 1947	Right 10	Jan. 11, 1946	Sailor	Games	Full	1
14	July 20, 1947	Left 7 Right 2	Dec. 12, 1945 Feb. 18, 1946	Builder's labourer	Football	Full Full	None None
15	..	Left 21	Dec. 19, 1945	..	..	..	Untraced

Digitized by Google

At follow-up a year or two later a full range of movement was found in 14 shoulders, a limited range in 1 (1 patient was not traced), and in 12 shoulders there had been no recurrence of dislocation.

SUMMARY

Recurrent dislocations of the shoulder-joint are due to a combination of structural and functional circumstances which should be considered in the planning of any operation.

Restoration of the normal synergistic action of the muscles by partial tenotomy of the subscapularis muscle, combined with an artificial increase of the articular area of the glenoid cavity, should give the highest percentage of cures with the normal range of movement.

An operation of this kind is described, and the results in 14 cases are tabulated.

I wish to thank Prof. T. P. McMurray who showed me, and was using, a similar principle in operating, and the Medical Director-General of the Royal Navy for permission to publish these cases.

REFERENCES

Bankart, A. S. B. (1938) *Brit. J. Surg.* **26**, 23.
Oudard (1924) *J. Chir., Paris*, **23**, 13.

EFFECT OF CARONAMIDE ON BLOOD-PENICILLIN CONCENTRATIONS IN MAN

R. B. HUNTER
M.B.E., M.B. Edin., M.R.C.P.E.
LECTURER ON THERAPEUTICS IN THE UNIVERSITY OF EDINBURGH

W. M. WILSON
M.B. Edin., F.R.C.P.E.
CRICHTON RESEARCH SCHOLAR

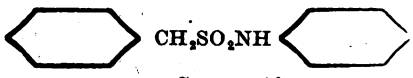
With the Technical Assistance of JAMES DICK

From the Department of Therapeutics, University of Edinburgh and the Clinical Laboratory, Royal Infirmary, Edinburgh

THE rapid excretion of penicillin by the kidneys has made it difficult to maintain constant therapeutic plasma-penicillin levels. Attempts to do so have been made in different ways—e.g., by giving frequent intramuscular injections, by using oily media to delay the absorption of penicillin (Romansky and Rittman 1944), and by trying to delay the excretion of penicillin by the renal tubules.

Some 80% of the penicillin which appears in the urine has been excreted by the tubules (Rake and Richardson 1946), and its excretion by this route can be delayed by diodone (Rammelkamp and Bradley 1943), *p*-aminohippuric acid (Beyer et al. 1947), or sodium benzoate (Spaulding et al. 1947). Beyer (1947) suggests that these substances functionally saturate the renal tubules and thus inhibit the elimination of penicillin. Their application to therapeutics is limited, however, because they are excreted as rapidly as penicillin, and hence it is only possible to maintain adequate concentrations by their continuous intravenous administration.

Beyer (1947) has reported that the tubular excretion of penicillin can be reversibly inhibited by the administration of a compound synthesised by Sprague et al. (see Beyer et al. 1947) and marketed in this country under the trade name of 'Caronamide':



Caronamide
(4'carboxyphenylmethanesulphonanilide)

It was claimed that, though this compound could block the tubular excretory mechanism for penicillin, it was eliminated from the body by slow glomerular filtration. It was absorbed from the alimentary tract and could be given by mouth in sufficient quantities to produce its effect on the tubules. In animals its administration led to no detectable tubular damage and to no significant alteration in the blood chemistry or in the glomerular filtration of urea or of sulphonamides. When the administration of caronamide was stopped, there was a rapid return of tubular function to normal, even after caronamide had been administered for several weeks. Tubular reabsorptive mechanisms, such as those for glucose, were unaffected during its administration.

Beyer's conception of the mode of action of caronamide was that it inhibited some enzymatic component of tubular excretion and thereby blocked the particular system involved in the excretion of penicillin. The inhibition by ephedrine of tyramine deamination by amine oxidase is cited as a parallel in-vitro inhibition.

Crosson et al. (1947) studied the effects of the administration of caronamide to persons receiving penicillin by intramuscular injection and by mouth. They found that the blood-penicillin levels were raised to 2–7 times greater than during the control periods. Seeler et al. (1947) found that when caronamide was administered in doses of 2 g. four-hourly to patients over 60 years of age there was a pronounced increase in the plasma-penicillin levels. It appeared necessary to give 4 g. four-hourly to younger persons to produce the same effect; but, when this dose was given, the blood-penicillin levels produced by the injection of 100,000 units of penicillin were higher than those produced by the injection of 300,000 units without caronamide. Boger et al. (1947) confirmed the action of caronamide on penicillin excretion in man. With caronamide they maintained plasma-penicillin levels of 30–60 units per ml. They found, however, that the effect of the same dose was not always constant in the one patient at different times.

Dosage.—Enough caronamide has to be given daily to inhibit tubular function adequately. Methods devised for the estimation of plasma-caronamide are not practical for routine use, but from experimental studies it seems necessary to attain plasma-caronamide levels of 20–30 mg. per 100 ml. (Boger et al. 1947). Probably the effective dose varies somewhat from patient to patient according to the individual renal function, but in most cases 20–24 g. in twenty-four hours will produce the required blood-caronamide level and leads to significant tubular inhibition. In children it may be necessary to use the adult dose to produce the required effect.

Phenolsulphonephthalein Test.—Phenolsulphonephthalein is excreted by the same tubular mechanism as penicillin, and the administration of caronamide leads to a considerable decrease in the excretion of the dye during the first hour following its intravenous administration. It has been claimed that, if sufficient caronamide is given to inhibit tubular excretion of the dye, the excretion of penicillin is also inhibited (Boger et al. 1947).

CLINICAL STUDY

Our experiment was designed to determine the effect of caronamide on the blood-penicillin levels which can be achieved by repeated three-hourly or four-hourly injections, by a single injection, and by penicillin given by mouth.

Except where otherwise indicated all the patients were men, aged 20–52, convalescent from acute infections or conditions such as sciatica, and in none of them was there any evidence of renal impairment. They all received a standard hospital diet with no restrictions regarding salt or fluid intake. Penicillin was given intramuscularly as the sodium salt dissolved in normal saline solution at a concentration of 50,000 units per ml., and by mouth as the calcium salt. All the patients were given caronamide 3 g. three-hourly, one dose being omitted during the night, so that a total of 21 g. was

Digitized by Google

taken in the twenty-four hours; the drug was dispensed in 0·5 g. tablets. In all cases, except where otherwise indicated, this dose of caronamide was given for twenty-four hours before its effect on blood-penicillin levels was determined. Phenolsulphonephthalein-excretion tests, blood-ureanitrogen estimations, and urine examinations were carried out before and during caronamide administration.

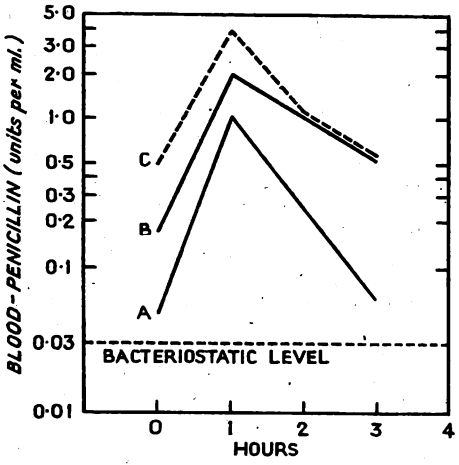


Fig. 1—Effect of caronamide on blood-penicillin levels when intramuscular penicillin 100,000 units is given three-hourly (logarithmic curves): A, before caronamide was given; B, after 24 hours' administration of caronamide; C, after 48 hours' administration of caronamide. Note increased effect on third day.

RESULTS

Repeated Intramuscular Injections of Penicillin.—The effect of caronamide in raising the blood-penicillin levels was determined in 6 cases in which repeated injections of penicillin were given three-hourly or four-hourly. The plasma-penicillin levels were estimated by the method described by Mackie and McCartney (1948). Of the 6 patients 5 had syphilis and 1 bacterial endocarditis. Fig. 1 shows a typical example. It will be noted that curve C obtained after forty-eight hours' caronamide therapy, is significantly higher than curve B, which was recorded on the second day. The detailed results in the other cases are given in the accompanying table. Fig. 2 shows the effect of caronamide administration on the four-hourly injections of 200,000 units of penicillin. The blood-penicillin levels achieved with a single injection of 500,000 units of penicillin are interpolated (curve C), and it is evident that the levels achieved with 200,000 units of penicillin with caronamide are greater than those produced by the single injection of 500,000 units without caronamide.

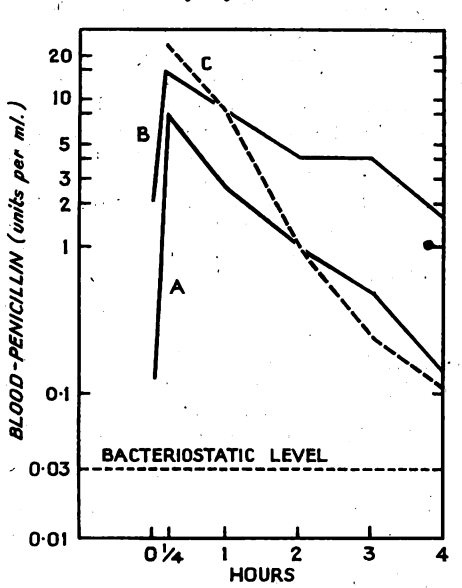


Fig. 2—Effect of caronamide on blood-penicillin levels: A, blood-penicillin levels when intramuscular penicillin G 200,000 units is given four-hourly without caronamide; B, readings from the same case after caronamide had been given for 24 hours; C, blood-penicillin levels achieved with a single intramuscular injection of 500,000 units of penicillin.

Single Intramuscular Injections of Penicillin.—In 10 cases caronamide was given to determine its effect on the duration of blood-penicillin levels following a single injection of penicillin. The phenolsulphonephthalein test was carried out on the first day of the experiment, and thereafter the blood-penicillin levels achieved by a single injection of penicillin were recorded (see table). From the second day caronamide 3 g. was given three-hourly until the end of the experiment. After twenty-four hours' administration of caronamide the dye test was repeated, and the blood-penicillin levels following the same dose of penicillin were again determined. When penicillin was demonstrable in the blood for more than six hours, the administration of caronamide was continued, and a further injection of penicillin was given next day. On this day the blood-penicillin levels were estimated 6–10 hours after the injection (see table). In 3 cases repetition of the phenolsulphonephthalein test twenty-four hours after the caronamide was stopped showed that tubular function had returned to normal. Fig. 3 shows a composite curve made from the average results obtained from 4 patients receiving intramuscular penicillin 100,000 units. It will be noted that the greatest effect is on the duration of the blood-penicillin levels, which are maintained for twice as long when caronamide is given. In 2 cases the blood-penicillin levels were not significantly raised. A similar finding has been reported by American workers (Seeler et al. 1947).

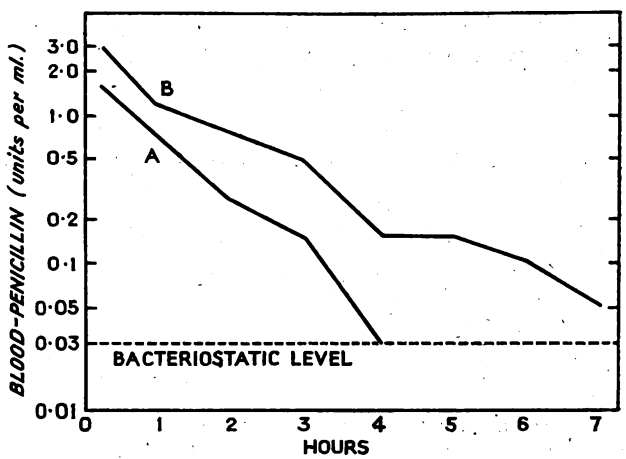


Fig. 3—Average readings from 4 patients given intramuscular penicillin 100,000 units: A, without caronamide; B, after caronamide had been given for 24 hours.

Penicillin by Mouth.—Recent experimental clinical studies have shown that not more than 35% of penicillin given by mouth appears in the urine (McDermott et al. 1946). It has also been shown that there is comparatively little destruction by gastric juice unless the pH is under 3 (Stewart and May 1947). Penicillin is probably absorbed in the upper part of the small bowel, being rapidly destroyed farther down the alimentary tract by penicillinase-producing organisms.

In our studies we did not try to neutralise the gastric acidity. All the patients had breakfast at 8 A.M., and calcium-penicillin powder, measured by weight, was given in a rice-paper cachet at 10 A.M. The other conditions of the experiment were essentially the same as those already described. Blood-penicillin levels following a single dose of penicillin by mouth were estimated on the first day and again after twenty-four hours administration of caronamide. Phenolsulphonephthalein tests were also carried out as described in the other experiments. The results are shown in the table. Fig. 4 gives a composite curve of the results obtained from 4 patients given calcium penicillin 50,000 units by mouth. When penicillin was given without caronamide

Digitized by Google

PLASMA-PENICILLIN LEVELS AFTER ADMINISTRATION OF PENICILLIN WITH AND WITHOUT CARONAMIDE

Case no.	Age (yr.)	Dose of penicillin (units)	Reduction in PSP excretion	Caronamide*	Plasma-penicillin levels (units per ml.) Hours after dose of penicillin											
					0	¼	1	2	3	4	5	6	7	8	9	10
Intramuscular Penicillin (Single Dose):																
3	49	30,000	54%	— C	.. ..	0·5 1·0	0·25 0·18	0·03 0·06	0 0	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
5	21	30,000	15%	— C	.. ..	1·0 0·5	0·5 0·5	0·03 0·06	0 0·09	.. 0·015	.. 0	.. ..	.. ..	.. ..	.. ..	.. ..
9	39	30,000	62%	—	..	Not done ..	..	0·125	0·09	0·06	0·06	0·03	0·015	0	..	..
12	26	30,000	Not done	— C	.. ..	0·5 1·0	0·25 0·5	0·06 0·25	0·03 0·125	0 0·09	.. 0·06	.. 0·015	.. 0·015	.. 0	.. ..	.. ..
7	50	50,000	46%	— C	.. ..	0·5 0·75	0·25 0·5	0·06 0·5	0·03 0·125	0 0·06	.. 0·06	.. ..	.. ..	.. ..	.. ..	.. ..
9	39	50,000	Not done	—	..	Not done ..	..	..	..	..	0·125	0·125	0·06	0·045	0·03	..
15	28	100,000	Nil	— C	.. ..	2·0 3·0	0·5 1·0	0·25 0·3	0·03 0·2	0·03 0·09	0 0·06	.. 0·045	.. 0·015	.. 0	.. ..	.. ..
16	26	100,000	90%	— C C	.. .. ..	1·5 4·0 ..	1·5 1·0 ..	0·75 1·0 ..	0·25 0·5 ..	0·06 0·25 ..	.. .. 0·37	.. .. 0·25	.. .. 0·125	.. .. 0·06	.. .. 0·03	.. .. 0·015
17	46	100,000	68%	— C C	.. .. ..	1·0 4·0 ..	0·5 2·0 ..	0·25 1·5 ..	0·125 1·0 ..	0·03 0·25 ..	0 .. 0·18	.. .. 0·125	.. .. 0·06	.. .. 0·03	.. .. 0·015	 0
18	28	100,000	Nil	— C C	.. .. ..	2·0 1·0 ..	0·5 0·5 ..	0·06 0·25 ..	0·03 0·09 ..	0 0·03 ..	.. .. 0·03	 0	 0	 0	.. .. ..	.. .. ..
4	49	200,000	66%	—	.. ..	8·0 22·0	1·0 2·5	0·5 1·0	0·125 0·25	0·06 0·25	0·03 0·25	0·015 0·1	0 0·1	.. ..	.. ..	.. ..
Oral Penicillin (Single Dose):																
1	35	50,000	90%	— C	.. ..	.. ..	0·25 1·0	0·06 0·25	0·03 0·125	0 0·125	.. 0·06	.. 0·03	.. 0	.. ..	.. ..	.. ..
2	47	50,000	65%	— C	.. ..	.. ..	0·03 0·125	0 0·015	.. 0	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
6	27	50,000	63%	— C	.. ..	.. ..	0 0·125	0 0·06	0 0·03	.. 0	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
10	46	50,000	29% 77%	— C C	.. .. ..	.. .. ..	0·03 0·06 ..	0·015 0·03 ..	0 0 ..	.. .. ..	.. .. 0·045	.. .. 0·03	 0	.. .. ..	.. .. ..	.. .. ..
8	52	100,000	70%	— C	.. ..	.. ..	0·25 0	0·06 0·03	0·06 0·03	.. 0·03	.. 0·015	.. 0	.. ..	.. ..	.. ..	.. ..
11	38	100,000	65%	— C C	.. .. ..	.. .. ..	0·03 0·18 ..	0 0·125 ..	.. 0·06 ..	.. 0·03 ..	.. .. 0·125	.. .. 0·06	.. .. 0·045	.. .. ..	.. .. ..	.. .. ..
13	45	200,000	Nil	— C C	.. .. ..	.. .. ..	0·18 0·5 ..	0·2 0·25 ..	0·125 0·125 ..	0·03 0·045 ..	0 .. 0·06	.. .. 0·03	.. .. 0·03	.. .. 0·015	 0	.. .. ..
14	43	200,000	38% 38%	— C C	.. .. ..	.. .. ..	0·125 0·03 0·25	0·03 0·03 0·125	0·03 0·03 0·06	0·015 0·015 0·03	0 .. 0·02	.. .. 0·015	 0	.. .. ..	.. .. ..	.. .. ..
19	35	200,000	Not done	— C	..	..	0·03 0·5	0·015 0·25	0 0·25	.. 0·06	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
Intramuscular Penicillin (Repeated Doses):																
20	25	100,000 3-hourly	Not done	— C	0·03 1·0	.. ..	0·5 4·0	0·125 2·0	0·03 2·0	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
21	30	,,	,, ,,	— C	0·06 0·5	.. ..	1·0 3·0	0·25 1·0	0·06 1·0	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
22	34	,,	,, ,,	— C	0·06 0·5	.. ..	1·0 3·0	0·25 1·0	0·06 0·5	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
23	40	,,	,, ,,	— C	0·06 0·25	.. ..	1·0 2·0	0·25 1·0	0·06 0·25	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
24	37	,,	,, ,,	— C	0·03 0·5	.. ..	0·5 2·0	0·125 1·0	0·03 0·5	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..
25	16	200,000 4-hourly	,, ,,	— C_4	0·125 1·5	8·0 16·0	2·5 8·0	1·0 6·0	0·5 3·0	0·125 1·5	.. ..	.. ..	.. ..	.. ..	.. ..	.. ..

* C, caronamide 3 g. three-hourly. C_4, caronamide 4 g. four-hourly.

Digitized by Google

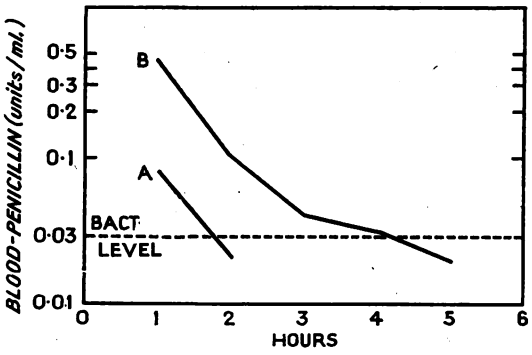


Fig. 4—Average readings from 4 patients given calcium penicillin 50,000 units by mouth: A, without caronamide; B, after caronamide had been given for 24 hours.

it was not present in the blood in detectable amounts for as long as two hours, but after caronamide had been given the blood-penicillin level was five times as high, and the effect lasted for four hours.

These results are so striking that it seems possible to us that caronamide may interfere with the destruction of penicillin in the alimentary tract besides delaying its excretion by the kidney. To clarify this point the urinary excretion of penicillin is being determined. The results will be published later.

Inhibition of Tubular Function.—Of 19 of the patients in this study, when the phenolsulphonephthalein test was carried out, 15 had a reduction of excretion in the first hour to less than 70% of the control reading. In only 1 of the 4 remaining patients were the blood-penicillin levels significantly altered. These preliminary observations suggest that the phenolsulphonephthalein test is a simple clinical guide to whether the excretion of penicillin by the renal tubules is being adequately inhibited.

Toxicity.—Of 24 patients who received an average dose of 60 g. of caronamide in two and a half days, none had renal damage as shown by a raised blood-urea-nitrogen level or by the appearance of albumin or of cellular elements in the urine.

Caronamide was invariably present in the urine in solution and could be precipitated by the addition of dilute acetic acid. The precipitate first appeared when the pH of the urine reached 5, and was maximal at pH 4. Because of the considerable acidity required for precipitation it is probably unnecessary to alkalinise the urine, but an adequate output of urine should be ensured.

In 22 of the 24 cases a substance was detected in the urine which reduced Fehling's and Benedict's solutions. Its exact chemical composition is at present unknown. Though it gives a positive Bial's orcinol test, reactions for glycuronic acid have been consistently negative (Rapoport et al. 1948); and, though it is likely to be a pentose, attempts to isolate the osazone have so far been unsuccessful. This substance appeared in the urine when caronamide was being given alone as well as during the administration of penicillin.

Of the 24 patients 2 complained of headache and 1 other of slight nausea. No drug rashes or drug fever were noted (cf. Boger et al. 1947).

DISCUSSION

Our findings are in agreement with the recent American work. They show that caronamide can be given by mouth in doses sufficient to delay the excretion of penicillin and to raise the blood-penicillin levels. Systemic toxicity is apparently low. There is no evidence of damage to the kidney, and the tubular inhibition is readily reversed by stopping the administration of caronamide.

It may be taken as axiomatic that all potent drugs are two-edged weapons capable of producing toxic effects. Unfortunately in the case of many preparations several years may elapse before these are clearly recognised. For this reason a drug which interferes with tubular function, no matter how harmless it may appear, should be used with caution. This is especially the case with caronamide because of the appearance in the urine of a reducing substance which is apparently a pentose and may well be a product of disorganised cellular metabolism.

For these reasons we suggest that, until caronamide has had a more extensive clinical trial, its use should be restricted to those cases in which the maintenance of high blood-penicillin levels is essential.

This study was suggested by Prof. D. M. Dunlop, to whom we are indebted for advice and criticism. We are grateful to Dr. Beyer, of Messrs. Sharpe and Dohme Ltd., Philadelphia, for the supplies of caronamide, and to Dr. H. M. Walker, of Glaxo Laboratories Ltd., for the supplies of penicillin.

REFERENCES

Beyer, K. H. (1947) *Science*, **105**, 94.
— Russo, H. F., Patch, E. A., Tillson, E. K., Shaner, G. (1947) *J. Pharmacol.* **91**, 272.
Boger, W. P., Kay, C. F., Eisman, S. H., Yeoman, E. E. (1947) *Amer. J. med. Sci.* **214**, 493.
Crosson, J. W., Boger, W. P., Shaw, C. C., Miller, A. K. (1947) *J Amer. med. Ass.* **134**, 1528.
McDermott, W., Bunn, P. A., Benoit, M., Dubois, R., Reynolds, M.E. (1946) *Science*, **103**, 359.
Mackie, T. J., McCartney, J. E. (1948) Handbook of Practical Bacteriology. 8th ed., Edinburgh.
Rake, G., Richardson, A. P. (1946) *Ann. N.Y. Acad. Sci.* **48**, 143.
Rammelkamp, C. H. Bradley, S. E. (1943) *Proc. Soc. exp. Biol., N.Y.* **53**, 30.
Rapoport, M., Corneal, F. B., Beyer, K. H., Verwey, W. F. (1948) *J. Amer. med. Sci.* **215**, 514.
Romansky, M. J., Rittman, G. E. (1944) *Science*, **100**, 196.
Sceler, A. O., Wilcox, C., Finland, M. (1947) *J. Lab. clin. Med.* **32**, 807.
Spaulding, E. H., Bondi, A. jun., Early, E. (1947) *Science*, **105**, 210.
Stewart, H. C., May, J. R. (1947) *Lancet*, ii, 857.

MASS DEATHS OF INFANTS

RÔLE OF CROSS-INFECTION

THILO BREHME
Dr. Med.
CHIEF PHYSICIAN, CHILDREN'S HOSPITAL, BRUNSWICK

THE possibility of cross-infection is a strong argument against nursing infants in hospitals. For this reason some authorities insist that babies should be nursed at home, and utterly condemn their admission to institutions. Not only does mass nursing help to spread cross-infection, but also it is possible that the pathogenicity and virulence of organisms in a hospital may be higher than they are outside, the continual change of patients leading to increased virulence by passage.

The incidence of cross-infection is most clearly shown by the mortality of children in hospitals. For instance, Van Ingen (1915) reported that of 28,210 infants under 2 years of age in foundling hospitals in the State of New York in 1910–15, 42·25% died, though the general mortality of infants in that State in the same age-group was only 8·7%.

EPIDEMIC DIARRHŒA

Since 1924, and to an increased extent since 1930, epidemics of diarrhœa with a high mortality have been reported from neonatal wards and nursing-homes. I experienced similar epidemics in 1939, 1940, and 1941 in a big lying-in section of a hospital. The characteristics of all these outbreaks were much alike.

Onset.—In the neonatal wards or nurseries, isolated cases of digestive trouble suddenly arose, the chief initial symptoms being refusal of food and changes in the stools. The disease then spread explosively like an epidemic. Some of the babies from the neonatal wards

Digitized by Google

fell ill after their discharge from the hospital nursery and were then admitted to the children's hospital.

Clinical Features.—These were usually refusal of food, vomiting (often intractable), and diarrhœa, sometimes with yellow stools. Later came collapse, signs of dehydration, increasing weakness, drowsiness, rapid loss of weight, and occasionally pyrexia, seldom rising higher than 102°F.

Course.—Usually the babies either died of toxæmia after two or three days at the latest or recovered after intensive treatment. In fatal cases there were increasing weakness, collapse, and failure of the circulation, often shown by severe meteorism. During the illness the weight of the babies often fell to 30% or even 40% below their birth-weight.

Age.—The age of the babies admitted to this clinic was 3–27 days, but most of the babies were aged 6–18 days when the first symptoms were observed. Newborn infants alone were affected, as other writers have pointed out. There was no difference in incidence among breast-fed, partially breast-fed, or bottle-fed babies.

Treatment in this clinic consisted in combating toxæmia: starvation, followed by special diet and supplemented by blood-transfusions. During the period of starvation carrot broth was given in preference to weak tea, because we believe carrot broth purges the intestine and absorbs toxins, besides providing a small amount of nourishment. The period of starvation lasted usually two or three days, sometimes longer, until a stage of detoxication was reached. Then we started giving buttermilk with 2% cornflour, at first without and then with 5% of a special sugar. Eventually a small quantity of breast-milk, partly skimmed, was given. As an adjuvant, especially in the period of starvation, we gave infusions of blood, or preferably plasma, eventually changing to 'Periston,' and saline plus the glucose either as a supplement or alternatively (20–40 ml. according to weight, sometimes twice a day). The average treatment in this hospital lasted about three weeks; elsewhere it had apparently been continued longer.

Prognosis generally depends on the virulence of the causal organism. This virulence may vary so much in different epidemics that, in assessing the value of any treatment, one must compare the results in epidemics of equal severity. A factor, which we had no opportunity of determining exactly, but which is also pointed out by Field et al. (1943), is that during the epidemic the case-mortality rises, until it may reach 100%; this is because the virulence of the organism is increased by passage. The case-mortality in different epidemics ranges from 12 to 80%, and it is usually not less than 50% when large numbers of infants are involved (Rice et al. 1937, Cooper 1937, Smellie 1939). In the three epidemics observed by me the rate was 22%; and, if the results from two other children's hospitals in Brunswick are included, it was 40%.

Ætiology.—Published opinions on the ætiology of the disease are not unanimous. Thus, Rice et al. (1937), Greenberg and Wronker (1938), Forbes and Olsen (1939), Roddy et al. (1939), Cron et al. (1940), Lembcke (1941), and I found that all bacteriological examinations, the search for a virus, the examination of food and stools, and the necropsy findings were completely without result. One epidemic Hotz (1932) ascribed to a *Staph. aureus* introduced by a nurse with an incompletely healed furuncle. Felsen (1939) accuses the Flexner bacillus; Cron et al. (1940) the hæmolytic streptococcus; Cooper (1937), Frick (1941), and Lyon and Folsom (1941), Pfeiffer's bacillus; Goebell (1943) *Proteus vulgaris* and *Ps. pyocyanea*; Cass (1941) *Bact. aerogenes*. In one epidemic observed by me *S. enteritidis* Gaertner was discovered; but in the other two epidemics we could not isolate any likely organism.

The high infectivity, the epidemicity, and the rapid spread of the disease suggest a virus of high pathogenicity perhaps closely allied to the influenza viruses. The organisms described by other writers should in my opinion be regarded as secondary invaders, or as symbionts with the true organism not yet discovered.

Young pigs are attacked by a sort of influenza starting with cough and bronchitis, soon leading to severe diarrhœa, and generally progressing so quickly and lethally that often 100% die. Farmers know that the infection is transmitted by droplets and that once sties are infected they are dangerous to new litters for long afterwards. They therefore use such sties for other animals before putting in young pigs again. This disease seems to resemble the gastro-enteritis of infants in some respects. Professor Wagener, of the Hygiene Institute, Veterinary High School, Hanover, informed me that the cause might in the first place be the conditions in the communal sties. Later Waldmann and Köbe (Riems) isolated a pneumotropic virus of the influenza group. Other bacilli found, such as *Bacillus bipolaris* and pasteurellas, would be regarded as only incidental. By improving conditions, and especially by avoiding communal sties, it is possible to get rid of the disease completely. Furthermore H. Hormann, in a paper on the ætiology of necrotic jejunitis shortly to be issued by the Bernhard Nocht Institute, refers to results obtained by Köbe in infectious gastro-enteritis in pigs, among which there have been severe epidemics, especially in young pigs. Thus there is in both cases an analogous condition in the rearing of animal sucklings.

The Japanese disease called "ekiri," seems to be a similar condition. This is an epidemic diarrhœa, especially attacking infants, and resulting in a case-mortality up to 80%. The clinical features include a very acute onset, high fever, collapse, cyanosis, and paralysis of limbs, followed by convulsions and unconsciousness, and eventually death. The causative organisms are believed to be of the *Bact. coli* or pseudo-dysentery groups. Adult contacts of babies suffering from ekiri often fall ill with a sort of dysentery.

PREVENTION

Combating an epidemic after it has broken out appears to be hopeless, and the unanimous opinion is that the infected hospital should be completely closed for a time. Prevention is therefore extremely important.

Field et al. (1943) recommended the accommodation of as few patients as possible in each ward; wider spacing of beds; face masks and surgical gowns for nurses; and immediate isolation of new cases of gastro-enteritis. In their view all children under 2 years of age admitted to hospital with dyspepsia should be nursed in isolation cubicles; if an epidemic of severe diarrhœa should break out, new admissions of infants should be stopped temporarily, as many infants as possible sent home, and the remainder widely distributed among older children and adults; and that homes for infants ought to be considered only as emergency war institutions. What a difference from the older view that neonatal wards should always be large!

Rice et al. (1937) emphasised the importance of aseptic nursing of all infants, including the sterilisation of all linen and food and a thorough disinfection of hands. Some writers have recommended that different nurses should be employed for feeding and for cleaning the babies, to prevent the transfer of organisms from the baby's anus to its mouth. Felsen (1939) even recommended the employment of a special epidemiologist. All these suggestions show that the prevention and combating of an epidemic are a grave problem, and that the pathogenicity of the germ must be extraordinarily high. In view of these circumstances, all authors emphasise the fact that temporary closure of the infected

Digitized by Google

institution is the only possible way of extinguishing an epidemic. With this my experience makes me agree.

EFFECT OF WAR

Such epidemics having already been observed in peace-time it is only natural that war should aggravate them. Steinert (1921) stated that from 1913 to 1916 in the foundling hospital in Prague mortality rose from 4·7 to 15·8%. The reasons why a war increases cross-infection are chiefly to be found in the following facts:

(1) The longer a war lasts, the more primitive conditions generally become, especially so far as they relate to children (cleanliness, lack of linen and soap, shortage of nurses, industrial employment of the mother, &c.).

(2) Modern war, particularly aerial war, and the employment of foreign labourers with their families, especially the employment of foreign women, lead to overcrowding of infants because of the establishment of numerous homes or hostels where babies and young infants, generally separated from their mothers, are inevitably exposed to the dangers of mass nursing, an accumulation of infections, and gastro-enteritis. People had forgotten how easily infants fell ill; and with the necessity for evacuating children as a protection against raids the consequences of such measures were at first lost sight of.

(3) With the mass movements of armies, evacuees, or displaced persons there was an increased exchange of bacteria among the population, leading to an increase in virulence by passage.

During the late war reports of German epidemics were not published, and, with few exceptions, foreign literature was unobtainable in Germany. In England Field and her colleagues (1943) reported a case-mortality of 80% among infants with gastro-enteritis at an emergency children's home. In June, 1946, Dr. Goebell wrote (private communication), that in Düsseldorf "many epidemics of gastro-enteritis are again raging in hospital nurseries, some with an enormous mortality." From a camp in Oksboel, Denmark, where many German refugees from East Prussia were accommodated I had news by letter that "all children under 2 years of age died of diarrhœa." The *Daily Mail* of May 29, 1946, reported that, in five ships carrying wives and babies of American soldiers from England to the U.S.A., a "mysterious illness" broke out, which appears to have been severe epidemic diarrhœa. The babies had assembled in a camp, where they awaited sea transport. Presumably conditions in that camp were not ideal, or the massing led to cross-infection. To prevent further damage the right decision was taken—to stop the transport of babies until they were older. Dr. A. Peiper reports (private communication) that he saw a severe epidemic of dyspepsia in newborn infants with at least 10 deaths in a short period during 1942–43 at Wuppertal. These were mainly breast-fed babies. The *Times* (Dec. 16, 1946) and the *Sunday Express* (Dec. 22, 1946) reported minor epidemics among babies, with a total of 30 deaths, which had occurred in Leicester (15 deaths) and other English cities. The morbidity was apparently somewhat higher, but figures were not quoted.

WAR NURSERIES IN GERMANY

Far more serious examples of cross-infection were noted in camps established for babies of displaced persons from the East by numerous armament factories all over Germany. The central authority (with an eye only to the labour pool) ordered that "in a simple but hygienic manner" homes were to be established for newborn and other babies of displaced persons from the East; that babies were generally to be looked after by women of the same nationality; and that the mothers should go to the hospital nursery not earlier than a few days before their confinement, and should resume work, at the latest three weeks post partum, when the newborn babies were to be brought into babies' homes. These orders, presumably drawn up without consulting a doctor, and certainly without the advice of a child specialist, did not take into account the consequences of overcrowding of infants separated from their mothers and looked after by insufficiently trained women. These orders led to cross-infection on a large scale, like a mass experiment, though it was not recognised as such by inexperienced doctors and still less by the laity.

EPIDEMIC DIARRHŒA IN INFANTS IN INSTITUTIONS

Authority	Year(s)	Place	No. of cases	Case-mortality (%)
Cohen et al. (1933)	1933	Brooklyn Hospital, New York	175	35
Rice et al. (1937)	1934–37	19 hospital nurseries in New York	505	46
Cooper (1937)	1937	Royal Children's Hospital, Glasgow	300	47
Greenberg and Wronker (1938)	1937	New York Babies' Home	52	23
Smellie (1939)	1939	Children's Hospital, Birmingham	500	10
Campbell and Cunningham (1941)	1937–39	Park Hospital, London	574	28
Brehme (1943)	1939–41	Ward for newborn, Landeskrankenhaus, Brunswick	53	42
Goebell (1943)	1939 1940	Various hospital nurseries, Düsseldorf	148 231	23 15
Brehme (unpublished)	1939–41	3 epidemics in Brunswick	129	40

After the end of the war I studied the conditions in four of these homes for babies of displaced persons from the East. The infants had been accommodated in huts, some of which were furnished quite adequately, but, though kept fairly clean, were often infested with bugs. There was a sufficient supply of medicine and appropriate food, but linen was rather scarce. The nurses were female displaced persons from the East, trained by German nurses. The doctors were very busy with other practice and were assisted by foreign doctors, medical students, or midwives. The children's home in Broitzemerstrasse, Brunswick, was staffed by foreign doctors only.

So far as the records could be obtained, the infants either developed furuncles and then died of sepsis, or, more usually, contracted a typical epidemic gastro-enteritis. The mortality in these homes was extraordinarily high in comparison with the figures usually accepted for nursing-homes before the start of this new phase of cross-infection, characterised by epidemics of gastro-enteritis of the newborn. Nevertheless, it is within the limits of the American, British, and German figures shown in the accompanying table. The mortality in four German homes for displaced persons studied by me was as follows:

Home	*No. of infants in home*	*No. of deaths*
Velpke	102 ..	89 (87%)
Wolfsburg	About 80 ..	About 45 (56%)
Rühen	„ 490 ..	„ 285 (58%)
Brunswick (May, 1943, to June, 1944)	351 ..	174 (50%)

The doctors and nurses in the homes repeatedly tried to get better results. Furunculosis was treated in the usual manner with lotions, ointments, dressings, and surgery. Bathing ill and healthy babies in the same bath, sometimes in the same water, unfortunately encouraged the spread of the boils and perhaps also of diarrhœa. Steinert (1921) expressly points out in his report that,

Digitized by Google

when infections, especially those of the skin, arise in the nursery bathing of babies must be stopped altogether, as the bath cannot possibly be properly disinfected. The need for the greatest cleanliness was repeatedly urged on the nurses, but perhaps not always properly observed by these inexperienced attendants, especially at night. Feeding difficulties were treated by careful dieting; drugs such as 'Tannalbin,' 'Rivanol,' and sulphonamides were used where indicated; food was given by tube to avoid vomiting; and infusions of saline and glucose were given. Severe cases from the homes at Wolfsburg and Rühen were sent to hospital. Attempts were made to identify the causal organism by bacteriological examinations of water, milk, and stools —but without success.

All this shows that in all four homes the true cause of the catastrophic consequences of nursing patients in these homes was not recognised; the risk of cross-infection was not properly appreciated. Thus doctors came to look on the mass deaths as inevitable and due to factors beyond medical control. The physicians of the four homes attributed the mass deaths to lack of mother's milk, insufficient adaptation of the infants to artificial feeding (Eastern European babies having for many generations been breast-fed), and innate lack of vitality, the result of the mother's working too long before her confinement, of her being insufficiently fed, and even of psychological influences (unwanted child, depression by separation from her country), and of attempts at abortion.

DISCUSSION

Mother's milk undoubtedly provides some protection against pyogenic infections, but in epidemics of gastro-enteritis the babies fall sick whether they are fed on the breast or artificially. The assumption that a newborn baby is less well adapted to artificial feeding because his parents and ancestors have been breast-fed contradicts not only the law of non-inheritance of acquired factors but also all experience.

To some extent the unborn child may be injured by the mother living in bad conditions during her confinement, perhaps also by psychological influences, but certainly not by attempts at abortion. The birth-weight of babies is lower in war-time than in peace-time, and the war baby's reserves of vitamins are certainly lower than normal, but on the whole the child grows in the mother's body like a parasite—i.e., it takes what is necessary for building its body if it is available.

The influence of mass nursing has been thoroughly misconstrued in these cases. The view of the physician in one of the homes is typical:

> "Taking the babies born with a lack of vitality and incapable of sufficiently adapting themselves to artificial feeding, had they been left to the individual care of their mothers, without being breast-fed by them, just as many of them would have died (though relatively fewer in special homes), simply because they were weak by birth and not accustomed to artificial feeding."

This is wrong; the truth is just the opposite. Reared in a family by their mothers (or other persons) they would have been endangered neither by cross-infection nor by gastro-enteritis of the newborn, even though they were artificially fed or their birth-weight was below normal owing to war conditions. It is tragic that such mistakes should have led to non-recognition of the true causes of the catastrophe and thus have contributed to the deaths of a large number of children.

SUMMARY

Cross-infection, previously believed to have been overcome, is still adversely affecting the results of nursing infants in homes.

It is chiefly responsible for the epidemics of infantile diarrhœa, which in many places have led to mass deaths in neonatal wards and infants' homes.

The information published up to now on this condition is tabulated, and the clinical features, course, treatment, prognosis, ætiology, and prevention are discussed.

The unfavourable influence of war on cross-infection is explained, with special reference to infants' homes for displaced persons in Germany.

The following suggestions are put forward:

(1) Homes and other large institutions for infants are permissible only in times of emergency, and even then they must meet all requirements with regard to equipment and nursing and medical staff.

(2) The healthy child should be born and reared in the family to avoid the danger of epidemic gastro-enteritis.

REFERENCES

Brehme, T. (1943) *Kinderärztl. Prax*, **14**, 1.
Campbell, R. M., Cunningham, A. A. (1941) *Arch. Dis. Childh.* **16**, 211.
Cass, J. M. (1941) *Lancet*, **i**, 346.
Cohen, H., Miller, P. R., Kramer, B. (1933) *J. Pediat.* **3**, 299.
Cooper, E. D. (1937) *Arch. Dis. Childh.* **12**, 339.
Cron, R. S., Shutter, H. W., Lahmann, A. H. (1940) *Amer. J. Obstet. Gynec.* **40**, 88.
Felsen, J. (1939) *Arch. Pediat.* **56**, 133.
Field, C. E., MacCarthy, D., Wyllie, W. G. (1943) *Brit. med. J.* **i**, 371.
Forbes, R. P., Olsen, F. B. (1939) *Arch. Pediat.* **56**, 250
Frick, P. (1941) *Mschr. Kinderheilk.* **87**, 70.
Goebell, O. (1943) *Ibid*, **89**, 70.
Greenberg, M., Wronker, B. M. (1938) *J. Amer. med. Ass.* **110**, 563.
Hotz, A. (1932) *Jahrb. Kinderheilk.* **135**, 129.
Lembcke, P. A. (1941) *Amer. J. Hyg.* **33**, 42.
Lyon, G. M., Folsom, T. G. (1941) *Amer. J. Dis. Child.* **61**, 427.
Rice, J. L., Best, W. H., Frant, S., Abramson, H. (1937) *J. Amer. med. Ass.* **109**, 475.
Roddy, R. L., Forrester, J. S., Landow, H. (1939) *Amer. J. Obstet. Gynec.* **37**, 1037.
Smellie, J. M. (1939) *Lancet*, **i**, 969, 1026.
Steinert, E. (1921) *Z. Kinderheilk.* **28**, 255.
Van Ingen, P. (1915) *J. Amer. med. Ass.* **65**, 79.

PARA-AMINOBENZOIC ACID IN LEUKÆMIA

EFFECT ON THE LEUCOCYTE-COUNT

H. B. MAY
M.A., M.D. Camb., M.R.C.P.
DIRECTOR OF CLINICAL LABORATORIES

J. VALLANCE-OWEN
M.A., M.B. Camb., M.R.C.P.
RESIDENT PATHOLOGIST

THE LONDON HOSPITAL

THOUGH leukæmia has been accepted as a neoplastic disease by Willis (1948) from considerations of morbid anatomy, and by Furth (1946) from experimental evidence, and though this view is supported by most hæmatologists, nevertheless the tissue-culture experiments of Israëls (1940) still hold out the faint hope that maturation of the leukæmic cell can proceed to the normal leucocyte under suitable nutritional conditions. To pursue this possibility we have used *p*-aminobenzoic acid, a well-established essential metabolite for many bacteria, in the treatment of leukæmia.

Five cases of chronic myeloid leukæmia, one of chronic lymphatic leukæmia, and one of acute leukæmia were treated.

Dosage.—The dose of *p*-aminobenzoic acid was related to that used in the treatment of rickettsial infections. All the patients received 0·5 g. per lb. of body-weight per 24 hours, divided into 2-hourly doses from 6 A.M. to 10 P.M. Blood concentrations were estimated daily by a modification of Bratton and Marshall's method for sulphonamides. Values between 60 and 100 mg. per 100 ml. of blood were obtained after the first 24–48 hours.

RESULTS

All five patients with chronic myeloid leukæmia showed a remarkable drop in the total leucocyte-count, irrespective of whether radiotherapy had been previously given or not. Within 21 days the total leucocyte-count could be brought in all cases to within normal limits,

Digitized by Google

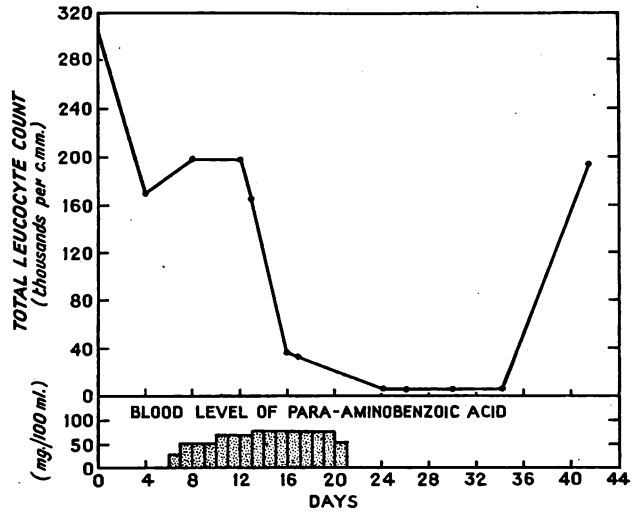


Fig. 1—Leucocyte-count in relation to blood concentration of *p*-aminobenzoic acid in chronic myeloid leukæmia.

but on cessation of treatment the count rose rapidly to its former value. Typical results are illustrated in figs. 1 and 2, and blood films before and during treatment in a typical case are shown in figs. 3 and 4.

After the count had returned to its former value a second course of treatment again produced a similar rapid fall. The differential count of the leucocytes in the peripheral blood and in the sternal marrow remained unchanged.

A case of lymphatic leukæmia with an initial leucocyte-count of 100,000 cells per c.mm. was treated for 15 days; and, although the percentage of polymorphonuclears in the blood decreased, the total leucocyte-count was unchanged.

A case of acute myeloblastic leukæmia was treated with full dosage, but the total leucocyte-count rose during treatment.

Other Effects.—In two cases the hæmoglobin content of the blood fell, in one case it remained constant, and in two cases it rose slightly, but the rise was negligible compared with that obtained when the patients were subsequently treated with radiotherapy.

Counts in all seven cases showed no change in the number of platelets.

In all five cases of myeloid leukæmia the spleen became appreciably smaller.

Toxic Symptoms.—To prevent acidosis the *p*-aminobenzoic acid was given as its sodium salt, produced by neutralisation with sodium bicarbonate. During treatment the plasma-bicarbonate was estimated daily. A drop of up to 20 c.cm. of CO_2 per 100 ml. of blood occurred in all cases, but no serious symptoms of acidosis appeared. All seven patients complained of slight nausea, but only one vomited. The most serious toxic effect was unexplained hæmorrhage, which did not appear to be due to a deficiency of prothrombin, vitamin C, or platelets. A tourniquet test did not reveal any increased capillary fragility. The tendency to hæmorrhage remained unexplained, but it was probably due to a local infiltration of the walls of small vessels with leukæmic cells, the vessels being also slightly damaged by the *p*-aminobenzoic acid. Two patients died, but at necropsy only the post-mortem appearances of death from chronic myeloid leukæmia were found.

DISCUSSION

Bichel (1948) treated six cases of chronic myeloid or lymphatic leukæmia with *p*-aminobenzoic acid and the leucocyte-count rose abruptly in all of them. Zarafonetis et al. (1948) treated five cases of chronic myeloid leukæmia and in each case obtained a profound drop in total leucocyte-count. Our results confirm the latter work. The discrepancy between Bichel's results and ours lies in the amount of the *p*-aminobenzoic acid given.

As in the growth of certain bacteria, *p*-aminobenzoic acid can act as a stimulus to cell division at low concentrations and as a depressant in high concentrations (Sevag 1946), an action similar to that of hydrocyanic acid and other poisonous substances. Our results were due to its effect not as an essential metabolite but as a toxic substance with a far higher toxicity for granular cells of the myeloid series than for cells of the lymphoid series or for very primitive hæmic cells.

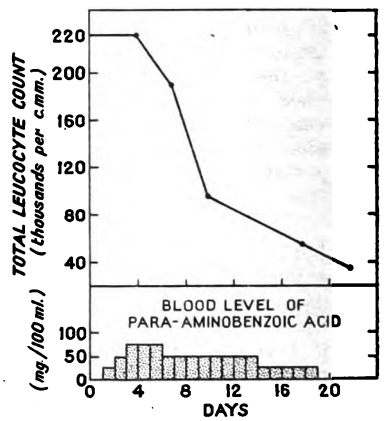


Fig. 2—Leucocyte-count in relation to blood concentration of *p*-aminobenzoic acid in same patient as in fig. 1 but on second admission three months later.

SUMMARY

p-Aminobenzoic acid caused a profound drop in the total leucocyte-count of the blood in chronic myeloid leukæmia when administered in doses of 50 g. a day.

The hæmoglobin content of the blood was also reduced but not so much as the leucocyte-count.

The patients' general condition was little affected, but toxic symptoms were occasionally severe.

The division of myeloid cells, like bacterial multiplication, appears to be stimulated at low concentrations

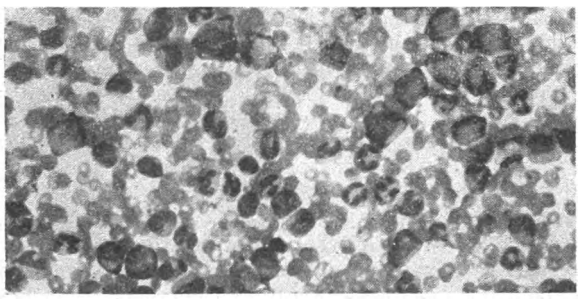


Fig. 3—Blood smear of patient with chronic myeloid leukæmia before treatment with *p*-aminobenzoic acid.

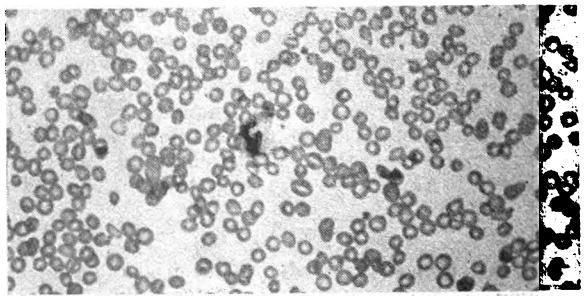


Fig. 4—Blood smear of same patient as in fig. 3, showing effect of *p*-aminobenzoic acid.

Digitized by Google

and depressed at high concentrations of *p*-aminobenzoic acid.

We wish to thank Messrs. Ward Blenkinsop and Co. for supplies of *p*-aminobenzoic acid, and Dr. R. R. Bomford, Dr. A. E. Clark-Kennedy, Dr. F. Ellis, Dr. Horace Evans, and Prof. C. Wilson for access to patients under their care.

REFERENCES

Bichel, J. (1948) *Nature, Lond.* **161**, 353.
Furth, J. (1946) *Physiol. Rev.* **26**, 47.
Israëls, M. C. G. (1940) *J. Path. Bact.* **51**, 235.
Sevag, M. G. (1946) Advances in Enzymology. New York and London; vol. VI, p. 53.
Willis, R. A. (1948) Pathology of Tumours. London; p. 793.
Zarafonetis, C. J. D., Andrews, G. A., Meyers, M. C., Bethell, F. H. (1948) *Blood*, **3**, 780.

DESPECIATED BOVINE SERUM

DAVID ANNIS
M.B. Lpool, F.R.C.S.
RESEARCH FELLOW IN SURGERY, DEPARTMENT OF SURGERY, UNIVERSITY OF LIVERPOOL

EDWARDS (1944), working in the Department of Surgery in the University of Liverpool, described a method of preparing despeciated bovine serum as a substitute for human plasma. Later he recorded its use in 200 cases (Edwards 1946). Since then Massons (1946) in Barcelona has reported favourably on the use of a very similar formol-ammonia-heat-prepared serum in 200 cases and in 1000 experimental injections. Mëlka et al. (1947) confirmed his experience, but Bing (1948) and Boesen et al. (1948) found that in serum prepared by the method of Massons the osmotic tension was reduced by 50% and that it was still capable of toxic and antigenic effects.

In Edwards's original method the serum was separated, diluted with water in the proportion of 4 parts of serum to 1 part of water, bacterially filtered, despeciated, and collected in sterile bottles. Despeciation was effected by adding formol and sufficient ammonia to convert the excess formol to harmless hexamine. This prevented coagulation during the next stage, when the serum was heated to 72°C for 30 min. Edwards considered that the despeciating factor was heating to 72°C and not the addition of formol and ammonia. He showed that the addition of these substances to bovine serum without heating did not lead to despeciation. Jacobs and Sommers (1939) had shown this to be true for many mammalian sera.

This work was carried further in this department to discover the chemistry of this change and the exact nature of the end-product. It soon became evident that the chemistry of formol proteins was very complex and ill understood, and that it would be difficult to prove that serum prepared by this method was protein of high molecular weight acting in every way like the human plasma proteins and therefore a satisfactory substitute for human plasma.

Because of these difficulties a simpler method of preparation without using formol was sought. Accepting Edwards's belief that heating to 72°C was the all-important despeciating factor, we looked for other methods of preventing coagulation on heating, and found it possible to avoid coagulation by adding, before heating the serum, sufficient sodium hydroxide to bring the pH to 9. The serum showed an exactly similar physical change to that described by Edwards, assuming a greenish opalescence and a slight fluorescence. In heating the serum we fulfilled the exact instructions laid down by Edwards, bringing the serum to 72°C by raising the water-bath temperature from 60 to 75°C as rapidly as possible and maintaining it for 30 min. The product was cooled and the pH returned to pH 7 by the addition of hydrochloric acid.

This at first sight appears to be a more simple method, gaining the same ends and avoiding the use of formol. Serum treated in this way lost its power of agglutination and hæmolysis when added to human blood.

Experiment I.—Serum was added in equal quantities to four batteries of 40 test-tubes each containing a sample of human blood of a different group or subgroup. At 2 hours and at 24 hours, both at room temperature and at body temperature, the tubes were examined. In no tube was there hæmolysis or agglutination. A similar control series with untreated serum led to agglutination and hæmolysis in every tube.

We were satisfied that the agglutinins and hæmolysins had been destroyed by this process.

To discover the composition of the product we submitted samples of the serum for electrophoretic and ultracentrifuge examinations at the Lister Institute for Preventive Medicine. The report showed that our product was far from satisfactory:

Report.—"It was obvious from the ultracentrifuge runs and by analysis of the plates that 90% of the protein was aggregated in the samples B and C, and this aggregated material sedimented to the bottom of the cell very rapidly when the rotor speed reached 20,000 r.p.m. The residual protein appeared to sediment, like normal albumin, at 60,000 r.p.m.

In the electrophoresis apparatus the normal plasma showed albumin and α, β, and γ globulin; but no fibrinogen was detectable. Both the despeciated samples appeared to consist electrophoretically of a single abnormal component essentially with a trace of albumin."

Protein osmotic tension was estimated at the Lister Institute by the method of Adair and Adair (1925). The sera were dialysed against *M*/15 phosphate buffer (*M*/30 KH_2PO_4 + *M*/30 $Na_2H\ PO_4$) of pH 6·8. The same buffer mixture was used as outer fluid in the osmometers, which were equilibrated for 14 days at 0°C. The osmotic pressures of the sera were measured in mm. of protein solution and calculated as mm. Hg after measurement of the densities by pyknomity at 0°C. This showed a protein osmotic tension of only a fifth of that of the original serum from which it was prepared:

	Osmotic tension (mm. Hg at 0°C)	*Density*
Normal plasma	10·63	1·0201
Despeciated plasma	1·97	1·0210

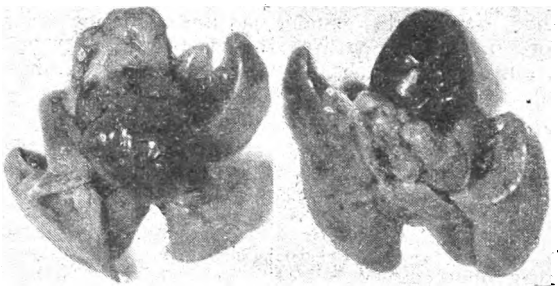
BIOLOGICAL EXPERIMENTS

The object of these experiments was to observe, by repeated injections, whether this prepared serum was truly despeciated—i.e., whether it had been rendered incapable of producing anaphylaxis. For this purpose we used three groups of guineapigs.

Group 1 we used as a control so that we might be well acquainted with the features of anaphylaxis in guineapigs. We injected two guineapigs intraperitoneally with 2 ml. of raw bovine serum as a sensitising dose, followed a month later by 5 ml. Both guineapigs manifested anaphylaxis within 5 min.; one recovered in 4 hours, and the other died a typical anaphylactic death.

Guineapigs are particularly suitable for this work, since they readily manifest easily recognisable anaphylactic phenomena when injected after being sensitised with foreign protein. In a sensitised guineapig, within 2–3 minutes of the intraperitoneal injection of foreign protein, in a full attack, the animal becomes stationary its fur becoming ruffled and erect, especially over the dorsal spine. The guineapig often emits sneeze-like sounds, and there is much nose-rubbing with the front paws. Often the guineapig becomes apparently ataxic and lies with both back legs outstretched, or it may fall to one or other side. Respiratory difficulty follows, with increasing difficulty in expiration.

Digitized by Google



(a) (b)

Fig. 1—Normal guineapig lungs and heart, showing collapse of lungs after removal from chest: a, anterior view; b, posterior view.

Group 2 consisted of four guineapigs which we injected intraperitoneally with 2 ml. of serum despeciated by our method of alkalinisation and heating, followed 30 days later by 5 ml. The results were as follows:

Guineapig 1: death from asphyxia in $2^1/_2$ hours.
Guineapig 2: no effect.
Guineapig 3: slight effects with recovery.
Guineapig 4: death in typical anaphylaxis within 10 min.

Necropsy in the two guineapigs which died showed a picture of anaphylactic death with gross overinflation of the lungs, these did not collapse after the pleural cavities were opened and indeed remained inflated after they had been removed from the thorax.

Thus we demonstrated conclusively that our method of preparation of the serum did not destroy the antigenic properties of the bovine serum. We had failed to produce a despeciated bovine serum by alkalinisation and heating to 72°C. We had produced instead a substance composed of one grossly abnormal protein, with an osmotic tension only a fifth of that of the original bovine serum, which was still antigenic and capable of producing anaphylactic death in guineapigs. Whatever despeciation is produced by Edwards's formol-ammonia-heat method it is not due entirely to the heating as Edwards thought. Therefore despeciation by Edwards's method is probably due in part to the formolisation and in part to heating.

Group 3 consisted of eighteen guineapigs injecting repeatedly with formol-ammonia-heat-prepared serum. The accompanying table shows that anaphylaxis developed in eight of the eighteen guineapigs; that it was of gross and undoubted nature in four guineapigs; and that one guineapig (no. 10), died in 45 min. in well-marked anaphylactic shock. Necropsy revealed undisputed evidence of anaphylactic death with gross inflation of the lungs (compare figs. 1 and 2).

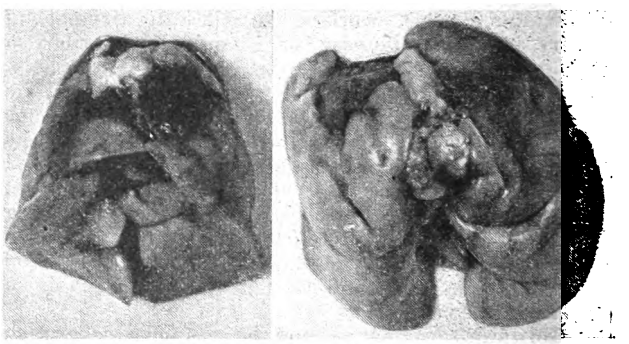
That only one of eighteen guineapigs died shows that serum treated by Edwards's method loses some antigenicity, carrying a lessened risk of producing anaphylaxis in guineapigs. Nevertheless these experiments show that it can still produce anaphylaxis and even anaphylactic death.

The guineapig is, of course, far more susceptible to anaphylaxis than man; but one cannot overlook the fact that, though such serum has been used without mishap in many hundreds of patients, its antigenicity and power to promote anaphylaxis are not completely destroyed by Edwards's method, and the potential danger still remains. With extensive administration of this serum to man, anaphylaxis will be seen. Caution should be exercised in its further use.

RESULTS OF REPEATED INJECTIONS OF DESPECIATED BOVINE SERUM IN GUINEAPIGS

Guinea-pig. no.	First injection (2 ml.)	Interval (days)	Second injection (5 ml.)	Interval (days)	Third injection (5 ml.)
1	Nil	35	Nil	59	Slight anaphylaxis
2	Nil	35	Slight anaphylaxis	59	Nil
3	Nil	35	Slight anaphylaxis	59	Nil
4	Nil	35	Nil	59	Died of pseudo-tuberculosis
5	Nil	35	Nil	59	Died of pseudo-tuberculosis
6	Nil	35	Nil	59	Nil
7	Nil	40	Nil	39	Nil
8	Nil*	..	..	..	..
9	Nil	40	Gross anaphylaxis	39	Nil
10	Nil	40	Nil	39	Died in well-marked anaphylaxis
11	Nil	40	Slight anaphylaxis	39	Nil
12	Nil	40	Nil	39	Nil
13	Nil	40	Nil	39	Nil
14	Nil	40	Gross anaphylaxis	39	Slight anaphylaxis
15	Nil	40	Nil	39	Well-marked anaphylaxis
16	Nil	40	Nil	39	Nil
17	Nil	40	Nil	39	Nil
18	Nil	40	Nil	39	Nil

* Died after 1st injection, with old infarcts in liver, probably from old age.



(a) (b)

Fig. 2—Guineapig lungs removed from chest after death in well-marked anaphylaxis, showing maintained inflation of lungs due to bronchospasm: a, anterior view, b, posterior view (same reduction as in fig. 1).

SUMMARY

The degree of destruction of specificity secured by Edwards's method of despeciating bovine serum is not due entirely to heating but to the formolisation and heating combined.

The specificity of the serum and its power of producing anaphylaxis are not completely destroyed by Edwards's method, and remain a potential danger in its use as a substitute for human plasma.

Any process likely to remove effectively the specificity of bovine serum is likely so to reduce its osmotic effects as to render it unsuitable as a substitute for plasma for administration to man.

I wish to thank Dr. R. A. Kekwick and Dr. E. F. McCarthy, of the Lister Institute of Preventive Medicine, for the electrophoretic, ultracentrifuge, and osmotic-pressure readings; Mr. W. Lee, of the central photographic department, University of Liverpool; and Mr. Harold Nevin, technician in the department, for valuable assistance.

REFERENCES

Adair, C., Adair, G. S. (1925) *Proc. roy. Soc.* series A, **108**, 627.
Bing, J. (1948) *Acta. med. scand.* **130**, 407.
Boosen, C. E., Larsen, V., Nielsen, Aa. K. (1948) *Lancet*, **i**, 325.
Edwards, F. R. (1944) *Brit. med. J.* **i**, 73.
— (1946) *Lancet*, **ii**, 437.
Jacobs, J. L., Sommers, S. C. (1939) *J. Immunol*, **36**, 531.
Massons, J. M. (1946) *Lancet*, **ii**, 341.
Melka, J., Rapant, V., Zapletal, B. (1947) *Ibid*, **ii**, 383.

Digitized by Google

p-AMINOSALICYLIC ACID

DETERMINATION IN BLOOD AND CEREBROSPINAL FLUID

W. KLYNE, M.A., B.Sc. Oxfd, Ph.D. Edin.
LECTURER IN CHEMICAL PATHOLOGY

J. P. NEWHOUSE, B.Sc. Lond.
RESEARCH ASSISTANT

POSTGRADUATE MEDICAL SCHOOL OF LONDON

LEHMANN [1] mentions the use of Ehrlich's *p*-dimethylaminobenzaldehyde reagent for the determination of *p*-aminosalicylic acid in blood, but gives no details. We have developed the following method using Ehrlich's reagent, which is based on Morris's [2] method for sulphanilamide. The method has given satisfactory results in clinical trials in this hospital.

METHOD

Reagents

1. *p*-Toluenesulphonic acid, 20 g./100 ml. 0·2*N* HCl.
2. Disodium hydrogen citrate solution, 0·75*M* (39·4 g. A.R. citric acid, dissolved in 188 ml. 2*N* NaOH solution, and diluted to 250 ml.).
3. *p*-Dimethylaminobenzaldehyde, 2 g. A.R. in 95% ethanol (100 ml.).
4. Sodium *p*-aminosalicylate standard. The anhydrous salt (11·4 mg.) or the dihydrate (13·8 mg.) is dissolved in 100 ml. water to give the equivalent of 10 mg. *p*-aminosalicylic acid/100 ml.

Procedure

Oxalated whole blood, 0·5 ml., or cerebrospinal fluid (C.S.F.), 1 ml., is measured into a test-tube, made up to 7 ml. with distilled water, shaken well, and stood 3 min. to lake. Next 3 ml. of 20% *p*-toluenesulphonic acid is added slowly with shaking, and the mixture is allowed to stand a further 5 min. and then filtered (Whatman no. 40 or 42 paper).

To 5 ml. of filtrate (which must be clear) are added 1 ml. of citrate buffer solution and 2 ml. of 2% *p*-dimethylaminobenzaldehyde reagent. The orange colour develops at once and is stable for some hours.

The colour is measured with a photo-electric photometer using a blue filter (e.g., Ilford no. 602). A reagent blank is used consisting of 1·5 ml. of *p*-toluenesulphonic acid, 1 ml. of citrate buffer, and 2 ml. of Ehrlich's reagent made up to 8 ml. with water.

Standards

Three standards are used, containing sodium *p*-aminosalicylate equivalent to 20, 10, and 4 mg. of *p*-aminosalicylic acid/100 ml. From the 10 mg./100 ml. standard 1, 0·5, and 0·2 ml. portions are each made up to 7 ml. with water, and 3 ml. of *p*-toluenesulphonic acid is added to each. Then 5 ml. portions of these mixtures are treated with 1 ml. of citrate buffer and 2 ml. of *p*-dimethylaminobenzaldehyde reagent. A calibration curve is constructed from the three standards, and the *p*-aminosalicylic acid content of the unknown is deduced from it.

RESULTS

Experiments in which *p*-aminosalicylic acid has been added to various body fluids in quantities equivalent to 20, 10, and 4 mg./100 ml. have given the following recoveries: plasma (oxalated) *cir.* 100%, whole blood (oxalated) *cir.* 80–90%, C.S.F. *cir.* 100%.

In two series of experiments added streptomycin (1000 µg./ml. plasma) did not interfere with the determination of *p*-aminosalicylic acid.

Since the colour reaction is a general one for primary aromatic amines, it cannot be used for the determination of *p*-aminosalicylic acid if other primary aromatic amino-compounds (e.g., sulphanilamide derivatives) are likely to be present.

1. Lehmann, J. *Svenska Läkartidn.* 1946, **43**, 2029.
2. Morris, C. J. O. R. *Biochem. J.* 1941, **35**, 952.

Reviews of Books

Fungus Diseases of the Lungs

DAVID T. SMITH, M.D., professor of bacteriology and associate professor of medicine, Duke University, North Carolina. Springfield, Ill.: C. C. Thomas. Oxford: Blackwell Scientific Publications. 1947. Pp. 59. 10*s.* 6*d.*

THE rapid advance of medical mycology has created a demand for monographs on the mycoses of individual anatomical systems. It is fitting that the first should be one on the fungus diseases of the lungs, which are probably the easiest, and certainly the most important, portal of entry for pathogenic fungi. Professor Smith's little book (no. 2 of the American Lecture Series) describes, adequately but briefly, the symptoms, clinical and mycological diagnosis, and treatment. A conflicting statement needs correction: the remark that "the lungs are rarely, if ever, the site of primary infection" in histoplasmosis is followed two pages later by a reference to "tens of thousands of primary pulmonary infections" in this disease. Such slips do not, however, detract from the value of a useful guide to a group of pulmonary disorders all too often misunderstood. It is to be hoped that Dr. Smith will expand this work into a much-needed book of reference.

Symposium on the Use of Isotopes in Biology and Medicine

Madison: University of Wisconsin Press. 1948. Pp. 445. $5.

THIS book is the report of the symposium held at Madison, Wisconsin, in September, 1947. It was produced as quickly as possible, by a photolithographic process, and the various authors had no opportunity for proof-reading; but there are few errors, and a comprehensive list of errata is provided. The subjects discussed are all of topical interest and the articles are in the form of short reviews arranged in good logical order. The historical background for isotopes in biochemistry is given by Hans T. Clarke. Urey and Seaborg write of the separation of stable isotopes and the preparation of radioactive isotopes respectively. Nier discusses the mass spectrometer, and Coryell and Kamen the detection and measurement of radioactivity in radioactive isotopes; and there is a series of articles on the use of tracers in research on the metabolism of proteins, carbohydrates, lipids, and minerals. The medical applications of radioactive tracers, both for physiological and therapeutic use are considered at some length. Moreover, the measures to be taken to protect the health and property of the users of radio-isotopes are not forgotten. This report should be invaluable to those about to enter on investigational work with radioactive or stable isotopes, and to those with some experience in this field the articles will certainly be of interest.

Vitamine und Vitaminetherapie

Prof. Dr. Med. EMIL ABDERHALDEN, director of the physiological chemical institute, University of Zurich; Prof. Dr. Med. GEORGES MOURIQUAND, director of the Children's Hospital, University of Lyons. Berne: Huber. 1948. Pp. 408. Sw. fr. 28.

THIS is the first of a series of therapeutic handbooks to be published under the general editorship of Prof. T. Gordonoff of Berne. The object of the series is to provide, in nine relatively small volumes, each written by two or three experts, authoritative modern information. Professor Abderhalden has written the historical and biochemical part of this volume (188 pages) and Professor Mouriquand the clinical section. The first part carries a historical survey followed by more detailed treatment of each of the vitamins of the B complex, the fat-soluble vitamins with their provitamins and analogues, and the essential fatty acids and amino-acids. This section is copiously illustrated by photographs and structural formulæ, and closes with tables of vitamin food values and human requirements. In the second part Mouriquand distinguishes exogenous and endogenous—or as we would say "conditioned"—deficiencies due to diseases of the

Digitized by Google

gastro-intestinal tract, the liver, and other organs, and discusses the outstanding clinical diseases due to the specific vitamin deficiencies, and their treatment.

The book is good and moreover has balance, which might well have been lacking in the joint work of a German biochemist and a French clinician. The first part is on the whole well documented, though with an understandable bias towards German and Swiss publications. No volume of this size can claim to mention everything connected with the subject, but it is a little surprising to find vitamin D_2 dismissed so summarily, and no reference made to the work of Harris and Moore in the late 'twenties on hypervitaminosis D. Phytic acid is not mentioned at all, and the section on resistant rickets and osteomalacia is distinctly dated, showing no grasp of the recent Anglo-American work on treatment. There are none of the vivid clinical descriptions which one expects of a French writer, and some of the photographs are disappointing. It is, however, easier to criticise than to create, and those who read German will value this book, since parts of it are probably better than anything current in English.

Lehrbuch der inneren Sekretion

F. VERZÁR, professor of physiology, University of Basle. Liestal: Ars Medici Lüdin. 1948. Pp. 609. Sw. fr. 52.

Professor Verzár has written a comprehensive and authoritative textbook on endocrinology primarily from the physiological point of view. The bibliography is full, and especially valuable to the English reader because it contains many Swiss and Continental references with which he may not be familiar. The treatise is up to date and is a reliable reference work. It can be recommended to those who wish their library of orthodox endocrine publications to be complete.

Science in Progress

(Fifth series). Editor: GEORGE A. BAITSELL. New Haven: Yale University Press. London: Oxford University Press. 1948. Pp. 353. 27*s*. 6*d*.

THIS volume can be classified under the heading of Popular Science for the Scientist. The ten essays in it, reprinted from recent issues of the *American Scientist*, are too technical to be understood by the complete layman, but are of just the right level of comprehensiveness and precision to appeal to scientists in other fields. Most of the contributors' names are household words in the medical profession: Peyton Rous, writing on tumours; G. W. Beadle, on biochemical genetics with special reference to the bread mould neurospora; Michael Heidelberger on complement fixation; C. C. Speidel on the study of living cells; and Herbert M. Evans on the hormones of the anterior pituitary gland. Other essays (on the interior of the earth, for example, or the betatron) are written by authors equally well known in their fields. The standard of writing is high and the essays are well documented. It is a first-rate book, and can be particularly recommended to those whose stomachs revolt at the sort of popular science which contrives to be at once patronising, pompous, and imprecise.

Bergey's Manual of Determinative Bacteriology

(6th ed.) Editors: ROBERT S. BREED, New York State Experimental Station (Cornell University); E. G. D. MURRAY, McGill University, Montreal; A. PARKER HITCHENS, University of Pennsylvania, Philadelphia. London: Baillière. 1948. Pp. 1529. 82*s*. 6*d*.

BACTERIOLOGISTS will welcome this new edition of "Bergey," whose publication in the United States we have already mentioned (1948, i, 952). Nevertheless, those accustomed to our binomial system of bacteriological nomenclature may turn the pages a little anxiously; for in previous editions bacterial species have often been moved from one genus to another, adding confusion to a difficult subject. Seeking familiar names, we find that *Staphylococcus aureus* now has the clumsy designation *Micrococcus pyogenes* var. *aureus*; but most British bacteriologists will be glad that *Eberthella typhosa* has gone, and they may even agree that *Salmonella typhosa* is less likely to cause confusion with typhus than *Salmonella typhi*. There are many similar changes, and even if we regret unstable nomenclature we must recognise the new if we mean to read contemporary American and English literature. For the specialist there is something fresh in the presentation of the relationships of every genus, and the number of species has increased from 1335 in the fifth edition to 1630 in this. Particularly valuable is a new index stating which organisms have previously been recorded from a particular source. The orders Rickettsiales and Virales are in supplements: the viruses under the subgroups bacteriophage, plant, and animal viruses comprise 13 families, 32 genera, and 248 species. Taxonomy is becoming increasingly important, and the numerous contributors to this edition have done important scientific work.

Investigations on Agonal Acidosis

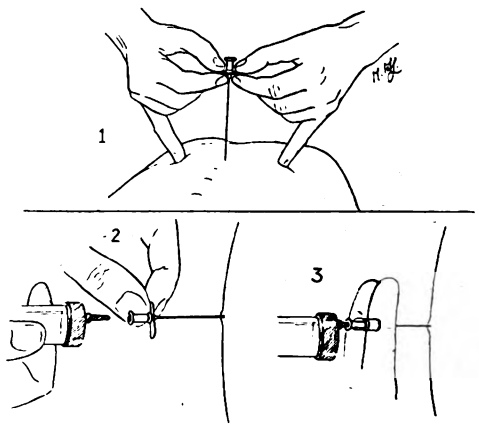
IB FABRICIUS HANSEN, translated by HANS ANDERSEN, M.D. Copenhagen: Poul Branners. 1948. Pp. 135.

THIS short book gives an account of the biochemical changes during the period immediately preceding death in man. On some 38 moribund patients Dr. Hansen has carried out examinations of the pH, carbon dioxide, chloride, urea, protein, hæmoglobin, oxygen, creatine, guanidine, amino-acids, lactic acid, pyruvic acid, serum sulphate and phosphate, total acetone bodies, total base, and non-protein nitrogen. Mean values of the various results are recorded, with full case-histories of each patient and a large bibliography. The main findings are a fall in blood pH immediately before death, with an increase in plasma lactic-acid content, which sometimes is very great. Most cases showed a terminal azotæmia with increased urea, amino-acid, and creatinine nitrogen values. No relation has been demonstrated between this azotæmia and the fall of pH.

New Inventions

A SPINAL NEEDLE

THE main object of the modification here described is to allow lumbar puncture to be performed without the point, shaft, or hub of the needle being touched. The needle is held throughout by two flanges which project at right angles at the junction of the hub and shaft. A two-handed stance allows counter-pressure to be



Figs. 1–3.

exerted by the little fingers on either side of the spinal column (fig. 1); in this way the needle is steadied and its direction controlled more easily.

If a spinal anæsthetic is to be given, the needle is held in situ by a flange while the syringe is being attached (figs. 2 and 3). By this means fingers are kept away from both the nozzle of the syringe and the hub of the needle.

The needles are obtainable in various lengths from $2^1/_2$ to 4 in., from the Longworth Scientific Instrument Co. Ltd., Thames Street, Abingdon-on-Thames, Berks.

R. R. MACINTOSH
Oxford. M.A., D.M. Oxfd, F.R.C.S., D.A.

Digitized by Google

To supplement nature...

'PROLUTON'

THE NATURAL PROGESTERONE

IN HABITUAL ABORTION

DYSMENORRHOEA AND

FUNCTIONAL UTERINE BLEEDING

2 mgm. 5 mgm. 10 mgm. in 1 c.c.
Boxes of 3 ampoules.

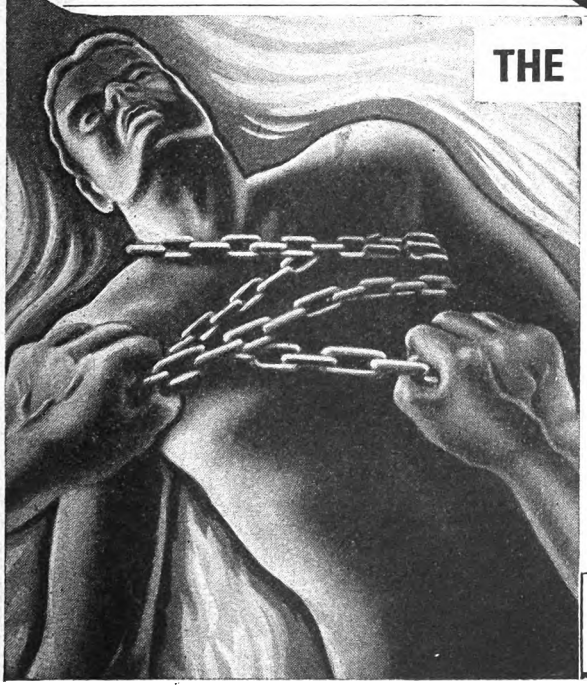
British Schering Limited

167-169 GREAT PORTLAND STREET, LONDON, W.1

22/H

BRONCHIAL ASTHMA

NEODRENAL
BRAND
ISOPROPYL ADRENALINE



THE NEW 'ORAL' ADRENALINE

A potent bronchodilator: well tolerated: prompt in action: adrenaline injections unnecessary: superior to ephedrine. Issued in the form of tablets for sublingual use and a spray solution for oral inhalation.

Literature and samples on request

A Product of the "SAVORY & MOORE" *Group*

SAVORY & MOORE LTD.
WELBECK STREET, LONDON, W.1

Digitized by Google

Introducing

'LYNORAL' ETHINYL ŒSTRADIOL

The most remarkable oestrogen known—

FOR ORAL ADMINISTRATION

DERIVED FROM THE NATURAL OESTROGEN

EXTREME POTENCY MEANS MINUTE DOSAGE

WITHOUT SIDE EFFECTS AT LOW TREATMENT COST

For all conditions where oral Œstrogen therapy is indicated

Scored tablets of 0.05 mg. · Tubes of 25 · Bottles of 100

Samples **and full literature on request**

ORGANON LABORATORIES LIMITED

BRETTENHAM HOUSE, LONDON, W.C.2

TELEPHONES: TEMPLE BAR 6785/6/7 0251/2 TELEGRAMS: MENFORMON, RAND, LONDON

'PERNIVIT'

Tablets of Acetomenaphthone and Nicotinic Acid B.D.H.

Considerable success in the treatment of chilblains has been reported following the use of acetomenaphthone in one group of patients and of nicotinic acid in a second group.

It may be that abnormal venous permeability and prolonged blood clotting time on one hand and venous stasis from vasoconstriction on the other may both be contributory causes of chilblains.

Trial of a combination of Acetomenaphthone and nicotinic acid collaterally, therefore, seems justified. 'Pernivit' is now available as tablets, each containing

Acetomenaphthone (Prokayvit Oral) **7mg.**
Nicotinic Acid **25mg.**

Bottles of 50 and 500 tablets.

MEDICAL DEPARTMENT
THE BRITISH DRUG HOUSES LTD. LONDON N.1
TELEPHONE: CLERKENWELL 3000 TELEGRAMS: TETRADOME TELEX LONDON

Prvt/E/525

Digitized by Google

THE LANCET

LONDON: SATURDAY, OCT. 16, 1948

First Quarter

GENERAL practitioners in the National Health Service have now received their first quarterly payment. Few have read the figures on their cheques with any satisfaction: most have felt that the work already done (to say nothing of busier quarters to come) deserved greater reward. As remuneration is calculated on the basis of an 18*s*. capitation fee for 95% of the population, and as it was unlikely that in the first three months so many as 95% would register, many doctors expected the first quarter to yield a comparatively high per-capita payment. Yet in most areas it has been less than 4*s*.

Several factors have contributed to reduce the amount. In the first place, the first four days of July, which came before the appointed day, were not included: and four days is almost 5% of a quarter. Secondly, no payments have been made during this quarter for temporary residents: credits accruing from these will be paid in next quarter's cheque. More importantly, the executive councils, being still unaware of their final commitments, have generally erred on the side of caution in making the first interim payment; to cover later eventualities they have kept something in reserve which will not be distributed until the final settlement next year. By that time the position should be clearer. It is known, for example, that there has been a considerable duplication of names, chiefly through form E.C.1 being forwarded in respect of patients already included in old panel lists; and until each form is checked and cleared some inflation is bound to persist. Again, the number of likely claims for treatment of temporary residents cannot be exactly foretold; nor has the total of mileage points claimed yet been calculated. A margin must be left for all of these, and each margin further reduces the amount of the pool available for initial distribution. Calculations of this type always had to be made before National Health Insurance cheques could be paid, and, once the numbers of the insured population in an area had become relatively stable, no great difficulties arose, and no inordinate balance had to be kept back for final distribution. But there remains one problem where no precedent can be quoted and where the needs and the decisions have varied widely from area to area. This is the problem of the "basic salary," or fixed annual payment. So much has the demand for this payment varied, and so little has general guidance been possible, that executive councils have had to make their own arrangements: and where they have thought fit either to grant a high proportion of fixed payments, or to put into reserve an appreciable sum for the eventual discharge of these payments, the remaining capitation fee has been proportionately depressed.

The right of a doctor to be remunerated in part by fixed annual payment has been progressively modified. The Minister of Health originally intended such payment to be universal; but the profession successfully opposed his wish to pay everyone partly by basic salary, and Mr. BEVAN eventually agreed that the fixed payment should be made only to those doctors who opted for it. When doubt arose whether such an arrangement would work fairly in the absence of restrictions, he accepted the British Medical Association's proposal that the fixed payment should not be made without specific approval of the local executive council; and after consultation with our representatives he indicated to executive councils certain categories of doctors to whom it might most justly be granted, including the doctor starting a new practice, or working up a small one, and the doctor unable, through age or ill health, to do as much as in the past. Little exception could be taken to extra help being offered to any or all falling into these categories, but the Minister went further when he suggested that the fixed annual payment might be made wherever "a doctor's income can be shown to have dropped substantially as a result of the new service involving an element of hardship." It is this last proviso, and its different interpretation by different executive councils and local medical committees, that has given rise to widely differing decisions. Some of the councils have asked that the doctor claiming the payment shall reveal his total income from all sources, and this has led to the charge that the Government are insisting on a means test for members of the profession.

Actually it is the doctors themselves who have demanded this income declaration from their colleagues, for the very pertinent reason that it is they who are paying from their own moneys the basic salaries that are granted. In putting forward the universal fixed payment the Minister arranged for it to be a first charge on the local pool of money from which the local executive council would pay the practitioners in its area. This would have been reasonably fair. It would in effect have provided a kind of sliding scale giving a higher average capitation fee for the man with the smaller list. But when the universal fixed payment was abandoned, and an optional one was substituted, it was decreed that the capitation fee for those doctors asking for the payment should be reduced by a seventh, and it became evident that any doctor with less than about 2200 patients would draw more from the pool if he was given a fixed payment than if he was not. Seeing that he obtains this extra amount at the expense of his colleagues with the larger lists, many local medical committees have refused to support applications unless they are satisfied that there is good reason for the claim. Some insist that the claimant shall reveal all sources of income and prove actual financial hardship; they treat the claim as a request for charity and they impose a means test. In present circumstances it is certainly permissible to say that no claim should be granted unless the whole picture of the doctor's practice is known. Obviously it would be unnecessary and unfair to subsidise the income of a junior partner, with a short list, if he was mainly employed in helping one or more senior partners with long lists, for each of whose patients full

Digitized by Google

capitation fees were being drawn. It is to prevent such an abuse that some executive councils have ruled that a basic salary cannot be granted to one partner unless the other partners also accept this form of payment. A practitioner can fairly say: "I prefer to limit my list of patients to a number which enables me to give unhurried service to them; in return for this I ask that I shall be paid proportionately more per patient, and so I claim the fixed payment." Before he does this he should be prepared to reveal the whole pattern of his practice so that the council may be assured that the time saved by having a shorter list can in fact be devoted to his panel patients, and will not be absorbed by paid appointments at clinics or hospitals, or by attention to an excessively large proportion of private patients. On the other hand for an executive council to declare that the doctor with private means or a wealthy wife shall be excluded from a method of payment that could legitimately be claimed by another practitioner, doing identical work, is wholly improper. The basic salary should not be regarded as a sort of alms, provided obligatorily by the busier doctors, to be doled out to the deserving poor among their colleagues, but as a means of obtaining sound conditions of practice, for doctors and patients alike.

At the moment conditions of practice are not conspicuously sound, and it would be useful to have an assurance that defects will be quickly remedied where necessary. As things stand today, the general practitioners are certain that their first payment in no way fulfils the promise of the first Spens report, and few believe that adjustments in coming quarters, when all errors and omissions have been rectified, will bring their remuneration into line with the Spens recommendations. Moreover it has become painfully obvious that a universal capitation system, unless more carefully compensated, works to the disadvantage of many of the doctors with the highest standard of practice.[1] Difficulties and anomalies of this kind were bound to arise, and some of the problems will solve themselves; but we trust the Minister will recognise the need for an immediate review of the subject as a whole, either with the Negotiating Committee or by the Whitley Council. Such a review should cover not only the amount of remuneration but also the sources of its various fractions. There are strong reasons why the sums that are not paid universally—e.g., the mileage, the inducement payment, and the fixed annual payment—should come from a fund kept separate from the main capitation pool. The inducement fund is already a separate fund; the mileage used to be, and could be again. The fixed annual payment could, with even greater advantage, also be kept separate. If this were done, it could be financed partly from the main pool of those capitation fees (a seventh of his total) which the doctor foregoes when he opts for the fixed payments. But the doctor with the long list would no longer be able to complain that his capitation fee was being depressed for the benefit of colleagues unable or unwilling to care for so many patients.

A bad start has been made, but it has at least had the advantage of revealing possible causes of continuing dissatisfaction. These causes being revealed, the cure should not be difficult to find. It is very desirable that discussions should be successfully concluded in time to ensure that practitioners derive due satisfaction from the cheques they will receive in the New Year.

1. See *Lancet*, Aug. 14, p. 259.

News about Viruses

IN the United States, where this summer has seen a high though fairly localised incidence of poliomyelitis, the disease is now receiving nearly as much public attention as cancer. One result is that news of experimental findings are appearing in the lay press before publication in the scientific journals. This tendency, however, is not confined to America or to poliomyelitis, as a peripatetic correspondent[1] lately noted. No blame attaches to the research-workers, who as a rule have merely read a preliminary paper on their subject to a learned society; and certainly not to the press, which is there to supply what its readers demand. If there must be a moral it is that scientific journals are apt to be more cautious than enterprising in gathering news. The fact remains that we in this country first learnt of phenosulphazole, a sulphonamide active against viruses, from a press notice issued by Columbia University; and our first view of the poliomyelitis virus spreading up a peripheral nerve was in the pages of *Time*.

The activity of some antibiotics and sulphonamides against the large viruses of the psittacosis-lymphogranuloma group is now established, and there have been hints and suggestions in recent publications of the possibility of finding agents active against some of the main body of viruses outside that group. The work on phenosulphazole, done by Dr. SUBBAROW (who died in August) and his colleagues,[2] may provide the much-needed lead to guide us into this big field. The new drug is the sodium salt of N-(2-thiazolyl) phenolsulphonamide; trade name 'Darvisul.' It was one of many compounds developed at the Calco and Lederle laboratories in 1947 and "showed promise," apparently against the virus of western equine encephalomyelitis. During the last year it has been tested against "poliomyelitis." Here a word of caution is needed. The virus workers at Columbia University do not agree with those in most other laboratories as to the limits of the term "poliomyelitis virus." SUBBAROW et al. have studied the Columbia-SK strain, which infects various rodents and differs from orthodox poliomyelitis viruses in its high infectivity by the intraperitoneal route and in other ways. Most workers believe it is of cotton-rat or mouse origin and not closely related to human poliomyelitis though a member of the same broad family group. The protocols show a high rate of survival in infected mice injected with 4–8 mg. of phenosulphazole two or four times a day over five days. A survival-rate of 100% was obtained only where the mortality in controls was well under 100%; but in one group 17 out of 20 treated mice survived for fourteen days where all of 20 controls died. Numerous recorded tests gave similar results. Surviving mice were subsequently immune to reinoculation. Such results were obtained when treatment was begun

1. *Lancet*, Sept. 18, p. 472.
2. Sanders, M., SubbaRow, Y., Alexander, R. C. To be published.

Digitized by Google

twenty-four hours after infection. In two experiments mice were given a single dose by mouth before infection, and more than half survived though all controls died. The drug is said to be "strikingly non-toxic" in mice and monkeys. Tests have been done on monkeys infected with poliomyelitis of human origin but the results are not reported. Apparently phenosulphazole does not react with the SK virus in vitro but inhibits its growth in tissue-cultures. It is argued from this that its action is on the cell, not the virus. Surely this is an odd conclusion, for various drugs inactivate bacteria only during their active growth and viruses can only grow in living cells. A particularly important point is that the drug's activity is inhibited by *p*-hydroxybenzoic acid (the effect of *p*-aminobenzoic acid is not stated).

The picture in *Time* [3] is copied from an electron photomicrograph shown by E. DE ROBERTIS and F. O. SCHMIDT of the Massachusetts Institute of Technology at a meeting in Canada. This photograph of a piece of the sciatic nerve of a rhesus monkey is said to show the poliomyelitis virus in the nerve. Earlier work has demonstrated the remarkable selectivity of this virus for neurons and suggested that it probably spreads centrifugally within the axoplasm of peripheral nerves. BODIAN and HOWE,[4] using the immersion method of inoculation of the cut end of the sciatic nerve in the rhesus monkey, showed that after a latent period of eleven hours the virus progressed up the nerve at about 2·4 mm. per hour. They tested for the presence of virus at different levels by inoculating nerve intracerebrally into monkeys. According to the report, DE ROBERTIS and SCHMIDT have observed bodies in poliomyelitis-infected sciatic nerves of the monkey which were not seen in healthy nerves; and serial pictures revealed movement of these bodies up the nerve at the same rate as BODIAN and HOWE found for live virus. It has long been recognised that the virus causes negligible disturbance of axonal function as it moves along the nerves, but exactly how it progresses has not been understood. These new revelations of the electron microscope suggest that the virus flows passively along the exoplasm. Most of the previous studies of the size and shape of the poliomyelitis virus by filtration and the electron microscope have been on purified preparations of human stool or spinal cord. According to the filtration experiments, the virus either is a sphere about 8–17 mμ in diameter, or if it is asymmetrical, has a cross-section of this dimension. Both American [5] and Swedish [6] workers have found rod-shaped particles 15–35 mμ in diameter in purified preparations of infected human stools and spinal cords, but they have found similar particles in the stools of normal children living in non-epidemic areas. The preparations from "healthy" stools were not infectious for monkeys, which suggests that the rod-shaped particles in both preparations are flagella of bacilli or some other extraneous matter to which the virus may be firmly attached in the infected specimens. Recently LORING et al.[7] have concentrated the Lansing strain of virus obtained from infected cotton-rat brains in sufficient quantity to provide an antigen for a complement-fixation test. These advances in physicochemical methods of purification should eventually supply a preparation which will unravel this mystery.

3. *Time*, Sept. 20, p. 29.
4. Bodian, D., Howe, H.A. *Bull. Johns Hopk. Hosp.* 1941, **69**, 79.
5. Melnick, J. *J. Immunol.* 1944, **48**, 25.
6. Gard, S. Purification of Poliomyelitis Viruses. Uppsala, 1943.
7. Loring, H. S., Roffel, S., Anderson, J. C. *Proc. Soc. exp. Biol., N.Y.* 1947, **66**, 385.

Lymphocytes and the Adrenal Cortex

IN discussing the formation and destruction of lymphocytes earlier this year [1] we described the evidence brought forward, particularly by DOUGHERTY and WHITE, in support of the view that adrenal cortical hormones control the process of dissolution of lymphocytes, that this dissolution leads to the liberation of γ-globulin, and consequently that the adrenal cortical hormones can be said to be concerned with antibody liberation and possibly with protein metabolism. The hypothesis was received rather coolly, and more recent work has been in several ways contradictory. VALENTINE et al.[2] set out to observe the effect of adrenocortical hormones on the number of lymphocytes appearing in the thoracic duct lymph of cats. They were careful to use adrenal cortex extracts and not the synthetic desoxycorticosterone, since it has been shown that the so-called "sugar" corticosteroids (i.e., those with the oxygen at C_{11} and C_{17} positions) are the important ones for hæmatological effects. Nevertheless the expected diminution of lymphocytes was not found—in fact there was no significant effect at all.

There seems to be no doubt that adrenocortical hormones produce macroscopic and microscopic involution of lymphoid tissue. It is also clear that injurious stimuli cause similar changes, and that the effects do not appear in adrenalectomised animals. There is much evidence to show that adrenal cortical hormones will produce a lymphopenia in normal animals. Most of the results were obtained in rats or mice, which normally have 60–90% lymphocytes in their blood compared with 20–40% in man. However, there have been some significant findings in man. Thus HILLS et al.[3] gave a single dose of 25 mg. of pituitary adrenocorticotrophin to 8 normal persons and 38 patients with various diseases but all with intact adrenals; a definite reduction in the circulating lymphocytes followed. A similar course given to 26 patients with Addison's disease produced very variable results—the lymphocytes in the blood showed anything from a 31% increase to a 28% decrease—but a dose of 17-hydroxycorticosterone caused a definite lymphopenia in every one of 5 patients. It was also noted that if adrenocorticotrophin is given regularly for some days the lymphopenia disappears in 24 hours and may give way to a lymphocytosis; HILLS and his colleagues have no explanation for this result. On the other hand, the evidence that patients with insufficient adrenal cortex, as in Addison's disease, have an increase in circulating lymphocytes is highly equivocal. For instance, BAEZ-VILLASEÑOR and others [4] studied the blood picture in 100 patients with Addison's disease. They set the normal high level at 40% lymphocytes, with a normal leucocyte-count, and by this criterion 16% of their 28 untreated

1. *Lancet*, 1948, i, 412.
2. Valentine, W. N., Craddock, C. G. jun., Lawrence, J. S. *Blood*, 1948, **3**, 729.
3. Hills, A. G., Forsham, P. H., Finch, C. A. *Ibid*, p. 755.
4. Baez-Villaseñor, J., Rath, C. E., Finch, C. A. *Ibid*, p. 769.

Digitized by Google

patients and 48% of the patients maintained on desoxycorticosterone acetate had a lymphocytosis; but the "average" figures given for these groups show that the 40% level has only just been exceeded and most of the counts would hardly be regarded as abnormal. Others have had similarly unconvincing results.

The severest criticism has fallen on that part of the theory which connects the dissolution of lymphocytes with the release of globulin antibodies. LI and REINHARDT [5] gave adrenocorticotrophin to rats and found that the plasma globulin actually decreased, but the albumin increased; GJESSING and CHANUTIN [6] report similar findings; HOUGHTON et al.,[7] using cats and rabbits, were also unable to confirm DOUGHERTY and WHITE's findings. Again, it has been noted that increased serum globulin is not found in human diseases associated with lymphatic hyperplasia; NITSKE and COHEN,[8] for example, found no significant alteration in serum proteins in 12 patients with lymphatic leukæmia. FAGRAEUS [9] denies that lymphocytes have anything to do with antibody formation and points out that the changes in lymphocytes brought about by adrenocortical hormones occur in less than 12 hours, whereas most antibody formation takes place 48 hours after appropriate stimulation. It is the plasma cells, she says, that are important for antibody formation, and there is good evidence now that plasma cells are derived directly from reticulo-endothelium and are not modified lymphocytes. FAGRAEUS carried out in-vitro experiments with isolated fragments of rabbit spleen; she found that there was always more antibody in red pulp than in white pulp containing splenic follicles (malpighian bodies), and that the capacity of the red pulp to form antibodies varied with the number of plasma cells, especially immature types that were present.

The idea that the dissolution of lymphocytes caused by adrenal cortical hormones is concerned with globulin production in general and antibody release in particular must therefore be regarded as "not proven." This is a pity because we have so little firm information on the function of the lymphocyte. But such contradictions should remind us to bear in mind the possible fallacy of assuming that changes brought about by artificial and considerable changes of hormone concentrations represent the normal mechanism of control; we are in fact faced with the old difficulty of deciding whether observed changes are physiological or toxicological.

5. Li, C. H., Reinhardt, W. V. *J. biol. Chem.* 1947, **167**, 487.
6. Gjessing, E. C., Chanutin, A. *Ibid*, **169**, 657.
7. Houghton, J. S., Thatcher, J. S., Hiles, C. *J. Lab. clin. Med.* 1947, **32**, 1410.
8. Nitske, B. A., Cohen, P. P. *Blood*, 1947, **2**, 363.
9. Fagraeus, A. *Acta med. scand.* 1948, **130**, suppl. 204.

Annotations

MEDICAL RESEARCH COUNCIL

Viscount Addison, M.D., has joined the Medical Research Council as chairman in succession to Lord Balfour of Burleigh. Others whose appointments to the council were announced this week are: Sir George Schuster, who succeeds Sir William Goodenough as treasurer; Sir Frederic Bartlett, F.R.S., professor of experimental psychology in the University of Cambridge; Sir Howard Florey, M.D., F.R.S., professor of pathology in the University of Oxford; and Mr. Geoffrey Jefferson, F.R.C.S., F.R.S., professor of neurosurgery in the University of Manchester. The other members of the council are: Group-Captain C. A. B. Wilcock, M.P., Prof. P. A. Buxton, M.R.C.S., F.R.S., Prof. Sir Alexander Fleming, F.R.C.P., F.R.S., Prof. C. A. Lovatt Evans, F.R.C.P., F.R.S., Prof. R. A. Peters, M.D., F.R.S., Prof. J. H. Gaddum, M.R.C.S., F.R.S., Prof. H. P. Himsworth, F.R.C.P., and Sir Edward Mellanby, F.R.C.P., F.R.S. (secretary).

NUFFIELD FOUNDATION

Two of the objects of the Nuffield Foundation are well known to doctors. These are "the advancement of health" and "the care and comfort of the aged poor." But there is a further aim—namely, "the advancement of social well-being"; and under this broad canopy the third report [1] records new grants for work on such widely differing topics as agricultural policy and the development of the reflecting microscope. In the field of the social sciences support is promised for a study of group relations and an investigation into the social factors of town-planning.

> "Town-planning in the past," the report observes, "has taken account of sanitary needs, natural features, and æsthetic considerations, and has reached the concept of the 'master plan'; but knowledge of the social and economic trends which should provide the real basis for continued planned development consists mainly in wisdom acquired after the event."

The foundation is also supporting a study of the middle classes, with special reference to their recruitment—an intricate system of which little is known. Recruitment of another sort is to be examined by Prof. Aubrey Lewis at London University's Institute of Psychiatry. Professor Lewis is undertaking a long-term study of university candidates—accepted and rejected—with the aim of determining: (1) to what extent the existing and familiar practice of selection agrees with the results of psychological procedures; (2) whether, in those accepted, academic or psychological assessment agrees better with the students' examination results and later performance; and (3) what happens to those rejected, and how far their subsequent success or failure could have been predicted from the results of the psychological tests.

Medical research is being aided by two new grants. One is for the establishment of a hæmatological unit at Oxford, and the other is for a survey of the health and development of children born in one week of March, 1945, who at that time were observed in a study of maternity services organised by a joint committee of the Royal College of Obstetricians and Gynæcologists, the Population Investigation Committee, and the Institute of Child Health of London University. One of the most valuable functions which the foundation has undertaken is the encouragement, by fellowships and other awards, of the exchange of students, both senior and junior, within the Empire. The Dominion medical travelling fellowships are to be continued, with slight modifications, for a further seven years; and within the Dominions committees are to be set up to advise on local requirements. The foundation has also been instrumental in procuring, for doctors in outlying parts of the African colonies, the stimulus of periodic visits by consultants from Britain.[2]

The major part of the obligation to the welfare of the old is now discharged through the National Corporation for the Care of Old People, established last year jointly with the Lord Mayor of London's Air Raid Distress Fund. For income the foundation relies mainly on the capital fund of £10 million presented by Lord Nuffield, but as the scope of its work grows it can put to good use any

1. Report of the Trustees for the Year ending March 31, 1948. Issued from the foundation's offices, 12–13, Mecklenburgh Square, London, W.C.1.

2. See *Lancet*, 1948, i, 431.

Digitized by Google

additions to the auxiliary fund; and the report records a gift of £450,000 by Captain Oliver Bird for rheumatism or other medical research. In the trustees' introductory words:

> "The welcomed increase of State support for learning and research does not lessen the need for voluntary enterprise: neither does it decrease the importance of alternative sources of support if the principle—fundamental to a free and democratic society—is to be upheld that 'there should be room for more than one opinion and for more than one means of putting that opinion to the test.'"

MEDICAL FILMS

THE three medical film meetings held on Oct. 8, 9, and 11 by the Scientific Film Association [1] in conjunction with the International Scientific Film Congress in London made it clear that too many recent productions are comparable to unrevised laboratory notebooks and not to prepared lectures or articles. On Oct. 8 there was a reasonably good film from Australia showing neurological sequelæ of starvation; this was followed by a Danish one on the clinical examination of syphilitics; then by a Belgian film which was difficult to follow visually, and by an American film on the toxic effects of streptomycin which wasted time on introductory sequences and on demonstrating nystagmus which was not there. Dr. Margaret Fries's film on the psychological implications of observations of behaviour during the (pædiatric) clinic visit showed what a wonderful subject this is for a teaching film, but did not quite overcome the difficulties it presents. Mr. E. Gwynne Evans's film on the behaviour of the orofacial musculature in children opened up new and more intelligent diagnostic and therapeutic approaches to the problems of "adenoidal" and mouth-breathing children. Two other films illustrating cases of chorea and Friedrich's ataxia, were approved for their brevity and directness; for the omission of unnecessary introductory shots and distracting furnishings in the backgrounds, and because (nearly) everything in the commentary was illustrated in the films. The absence of choreic movements during sleep, a fact that clinicians have usually to take on trust, was well demonstrated, and the shots of the child after recovery gave the viewers an interest in her as a person as well as a case. This admirable new venture by the Wellcome Medical Museum should certainly be expanded.

Next day Mr. R. McV. Weston spoke on cinemicrography and showed four examples. The first was an excellent twenty-year-old Canti film of cells in tissue culture; the other films showed a progressive improvement culminating in the film of osteoclasts made by Mr. Weston in collaboration with Dr. Norman Hancox, of Liverpool University. The evident possibilities of this skilled technique should be exploited for larger audiences. Teachers of biology and physiology would welcome a fifteen-minute film on the behaviour of living cells in normal blood.

The lesson of the first day's meeting was that badly photographed and badly edited films cannot tell a story well, but the moral to be drawn from the discussion on the second day was that good photographic technique is not enough. The American Medical Association centenary film, *The Medical Motion Picture*, was followed by a recently finished British film, *Subtotal Hysterectomy*, shown as a text for discussion. The lighting and colour were first-class, but the case was an unfortunate choice for the tumour was so large that it was difficult to see the other organs; only once was any detail of surgical technique shown, and possible difficulties were not emphasised. The criticism that this operation is or should be rarely done led to the expression of a widely held view—that the potential audience is too small to justify the making of postgraduate surgical films, in view of the urgent need for improving the teaching of students and nurses. The meeting ended with the film *Introduction to Acute Inflammation*, made by Dr. Beckett, Dr. Hansell, and Dr. Moller when they were students at the Westminster Hospital. This film uses diagrams, colour, and microscopy, and is a good instrument for teaching.

The last meeting opened with an American film on peptic ulcer, followed by a short cartoon film by Giles, *Cautionary Tales about Sepsis*. Mr. E. Fife Clark, public relations officer to the Ministry of Health, outlined past and present films from his ministry and discussed the part the film can play in health education. Miss Mavis Englefield of the Queen's Institute of District Nursing, introducing the U.S. Navy film, *Bathing the Bed Patient*, made a plea for simple nursing training films for mothers who like to look after their sick and would like to do it better. Dr. Stanford spoke on the value of short films, and several of these were shown—on the foramen ovale, a Dutch film on D.D.T. poisoning, an English film on the Aschheim-Zondek test, another showing a case of Sturge Weber syndrome (ending with the child sitting on Dr. Parkes Weber's knee), and one telling nurses how to put on a mask. Dr. Bloemensthal, of Holland, introduced a film he has made on the development of the peritoneum—an ideal subject for animation.

The meeting brought out once again the value of polished technique, to ensure that the audience's interest is in the content of the film,[2] and the importance of having a clear idea of what the film is to say and to what audience. It is good to hear that the S.F.A. are arranging that some, at least, of the films seen will be available in this country.

THE NAMES OF BACTERIA

THE complexities of bacteriological classification can only be guessed at by the student who has to follow his textbooks, or by the clinician who must grasp the gist of laboratory reports; but the present multiplicity of authoritative nomenclatures is a trial for both of them. On one side of the Atlantic we have the radicalism of Bergey's Manual [3] (reviewed on p. 612), which has not hesitated to lay hands even on such an old enemy as *Staphylococcus aureus*; moreover its sixty contributors, like their predecessors, seem to have ignored much of the work done outside the American continent. On the other side the Medical Research Council follows a more conservative path in the new list of species [4] maintained in the National Collection of Type Cultures at Elstree, Herts. In general the List follows the familiar nomenclature of Topley and Wilson,[5] so that *Salmonella typhi* has not suffered a sea change, à la Bergey, into *S. typhosa*.

On points of detail, medical bacteriologists may express surprise and regret that neither publication recognises the species *Bacillus mesentericus* and *B. vulgatus*; in the past the name mesentericus has been given to different organisms, but most strains are now regarded as either *B. pumilus* or *B. subtilis*. *B. anthracis* retains its identity in spite of Nathan Smith's [6] view that it is a pathogenic variety of *B. cereus*. Synonymy is common in the genus Clostridium; the List prefers *welchii* to the Manual's *perfringens*, though neither is valid if the Bacteriological Code is strictly followed. Bacterium is used in the Manual as the generic name for gram-positive and gram-negative non-sporing rods of uncertain taxonomic position; in the List it is used in italics for coliforms (*Escherichia* and *Aerobacter* of the Manual) and related intestinal organisms, and in roman type

1. Programme and detailed list of films can be obtained from the association at 34, Soho Square, London, W.1.

2. Izod, A. C. Place of the Film in Medical Education. London, 1946; p. 12.
3. Breed, R. S., Murray, E. G. D., Hitchens, A. P. Bergey's Manual of Determinative Bacteriology. Baltimore, 1948.
4. List of Species Maintained in the National Collection of Type Cultures. *Med. Res. Coun. Memo.* no. 21. London: H.M. Stationery Office. 1948. Pp. 17. 9d.
5. Topley and Wilson's Principles of Bacteriology and Immunity. Revised by G. S. Wilson and A. A. Miles. London, 1946.
6. Smith, N. R., Gordon, R. E., Clark, F. E. U.S. Dept. Agric. Misc. Publ. no. 559. Washington, 1946.

Digitized by Google

as a dump-heap for gram-negative rods that cannot be placed elsewhere. In neither case is the use of this generic term intended to be part of a systematic classification. There is an undesirable tendency, in both the Manual and the List, to put too much stress on the source of the organisms in determining their taxonomic position. This is an unhappy result of the division of bacteriology into watertight compartments—for example that of the medical worker who knows nothing of plant pathogens, and that of the plant pathologist unfamiliar with the bacteriological flora of polluted water.

The staphylococci are still to be found under the letter S in the List (instead of under *M* as in Bergey), but the List has adopted a new, and so far unexplained, classification for them. Ten years ago, Dr. Cowan,[7] who is curator of the National Collection, published a scheme in which coagulase production (which correlates well with toxigenicity) was used as the main criterion for the species *pyogenes*, and, as was to be expected, this is adopted in the List. Pigment is given taxonomic value only in the coagulase-negative strains; the specific name *aurantiacus* is used for the gold colony form to avoid confusion with the well-known *aureus*, now included in the species *pyogenes*.

An attempt is made in the Manual to include bacteriophages and viruses in a systematic classification of bacteria. Phagus, the generic name used for bacteriophage, is easily recognised, but *Tarpeia premens* (common cold), *Erro scoticus* (louping-ill), *Hostis pecoris* (foot-and-mouth disease), *Scelus recurrens* (herpes simplex), and *Borreliota variolæ* (smallpox) are not likely to be found in English writings for some time to come. British workers are not yet attempting to classify the viruses, since little or nothing is known of their "systematics."

AUREOMYCIN

PENICILLIN and streptomycin, effective as they are in many infections, still leave gaps in the antibacterial spectrum; so the search for new antibiotics goes on. A new one, described by B. M. Duggar of Lederle Laboratories, is aureomycin, derived from a strain of *Streptomyces aureofaciens* and effective against numerous gram-positive and gram-negative organisms, including streptococci of Lancefield groups A, D, F, and G, *Strep. fæcalis*, *Bact. pneumoniæ*, *Streptococcus pneumoniæ* types I, II, and III, *Hæmophilus influenzæ*, and *Brucella suis* and *abortus*. The antibiotic has been obtained as a yellow crystalline hydrochloride which deteriorates rapidly in alkaline solution at room temperature. The "acute toxicity" of aureomycin when injected subcutaneously into mice is between 3000 and 4000 mg. per kg.; daily doses of 60 mg. per kg. by mouth and of 3 mg. per kg. parenterally are well tolerated in man. It is excreted in large quantities in the urine but does not penetrate the blood-brain barrier.

Aureomycin is as effective as penicillin in protecting mice against *Strep. pneumoniæ* type I but is inferior to penicillin against β-hæmolytic streptococcal infections. Clinical trials have been carried out by Prof. Perrin H. Long and his colleagues [8] at Johns Hopkins Hospital, Baltimore. The dosage given by mouth varied from 10 to 60 mg. per kg. of body-weight per day, in divided doses. Intramuscularly a total daily dosage of 3 mg. per kg., given six-hourly, was well tolerated, though there were signs of moderate irritation at the site of injection. Five patients with Rocky Mountain spotted fever seemed to respond to aureomycin in twelve to seventy-two hours, and a patient with chronic brucellosis had a negative blood-culture forty-eight hours after the start of treatment and remained afebrile and asymptomatic for the next two months. The antibiotic sterilised the urine of two patients with a paracolon infection. These numbers are very small and need extending for critical appraisal. There is no question of aureomycin being another penicillin, but if the claims made for it are confirmed it should prove useful, particularly for the control of brucellosis and urinary-tract infections.

7. Cowan, S. T. *J. Path. Bact.* 1938, **46**, 31.
8. Bryer, M. S., Schoenbach, E. B., Chandler, C. A., Bliss, E. A., Long, P. H. *J. Amer. med. Ass.* 1948, **138**, 117.

HOSPITAL ADMISSIONS IN THE NEW SERVICE

SOME idea of the effects of nationalisation on hospital admissions in London can be gained from the experience of the Emergency Bed Service, which is still worked by the King's Fund though now on behalf of the four Metropolitan regional boards. The work of the E.B.S. has been extended by the addition of fever-hospital admissions, responsibility for which was taken over from the L.C.C. on July 5. These, however, do not account for the 400% rise in the number of calls received. The rise has been mainly due to a great increase in acute cases. There have been many applications for the admission of chronic cases, though not the deluge that might have occurred: doctors evidently realised that the new service could not produce beds overnight. The total number of calls received in the first three months of the service was 10,974 (acute 8132; fevers 2842), and some 500 chronic cases were passed through the service to the hospital management committees' waiting-lists.

The use of the E.B.S. by doctors is optional—they are in no way barred from arranging admissions direct with the hospitals—so this sudden increase is not easy to explain. One possible explanation, and a disturbing one, is that doctors are finding it more difficult to get patients into hospital and so are calling on the E.B.S. for help in a larger proportion of cases. This view is supported by the difficulty which the E.B.S. is itself experiencing in placing patients. All the fever cases have been admitted and virtually all the acute cases, in spite of a quarter of them being over 60 years of age. The fever admissions have been fairly simple, requiring an average of only 1·5 calls per case. On the other hand, for every acute case admitted an average of 4 hospitals had to be asked, as against 2·7 for the corresponding period last year and 1·6 in 1939. This figure was reached in the healthy month of September, and the E.B.S. has so far borne the strain, albeit with more delays than heretofore; but the winter months will evidently tax its resources to the utmost. Meanwhile steps are being taken to establish branch admission offices outside Greater London. As far as possible these will be run by the existing staff of the hospital management committees, who are being given a short course at the E.B.S. office in London. The intention is to establish centres throughout the Metropolitan regions so that doctors can be sure of obtaining a bed for their patient if there is a vacancy anywhere in his region.

HOUSE COMMITTEES

THE position of house committees was one of the subjects considered on Oct. 6 when the Minister of Health met chairmen of boards of governors, of regional boards, and of hospital management committees. Among the points made were some that have lately been raised in these columns,[1] such as the recruitment of management committees from members of the house committees who have shown their worth, and the need for heads of departments to be given their rightful position of responsibility. We understand that it was also suggested that house committees would gain a wider outlook if some of their members actively participated in the work of the management committees. No doubt arrangements will vary with circumstances, and there may be places where, instead of appointing a house committee, it would suffice to appoint house visitors who would keep the management committee in close touch with its several hospitals.

1. *Lancet*, 1948, i. 643; Oct. 2, p. 535

Digitized by Google

Special Articles

CONDITION OF CHILDREN IN WESTERN GERMANY

A. P. MEIKLEJOHN
M.A., B.M., B.Sc. Oxfd
LECTURER IN NUTRITION, DEPARTMENT OF MEDICINE, UNIVERSITY OF EDINBURGH

LITTLE has been published on medical conditions in post-war Germany. Newspaper reports have been scanty and often conflicting. Consequently it has been difficult for anyone outside the country to get a clear impression of the state of health of the people. Particularly, a great deal of doubt and anxiety must exist about the health of the children. This paper, based on observations made during two recent visits to Germany,* has been written in the hope that it may help to relieve such uncertainties. This does not claim to be a precise scientific study but merely sets forth the observations and conclusions of one person who has recently seen and examined many German children.

Whenever health in Germany is discussed, it has become usual to think first of nutrition. It is therefore well to begin with a short account of the population and the origin of its food.

The present total population of the combined British-U.S. zones, excluding Berlin, is about 41,300,000. The population of the French zone is about 5,000,000. Of the population in the British-U.S. zones 80% are "non-self-suppliers" and therefore depend on the rations. Of these, about 9,000,000 are children up to the age of 18. There are about 1,000,000 children up to the age of 18 in the French zone.

Before the war the area now comprising the British and U.S. zones produced about two-thirds of the food needed to provide its whole population with an average of 3000 calories per head daily. But then the population was only 34,000,000. Now there are 7,250,000 more people to be fed (mainly refugees from the east). Consequently more than half the food for this population is now imported, even though they eat less.

In 1939 the crop of bread grains in the combined British-U.S. zones was about 5,700,000 tons. By 1946 it had fallen to 3,450,000 tons, mainly through lack of fertilisers. The potato crop was about 17,500,000 tons before the war but had decreased by 6,000,000 tons in 1946. Further, before the war about 1,000,000 tons of bread grains, 1,000,000 tons of potatoes, and 400,000 tons of sugar used to come from the east—and this no longer comes. All this explains why it was necessary to import about 4,000,000 tons of bread grains into the British-U.S. zones in 1947. The actual deliveries from German farms to the market in the year ending June 30, 1947, was 2,250,000 tons. Hence in 1946 and 1947 about two-thirds of the bread ration in the British-U.S. zones was from imported grains. About the same proportion of bread grains is imported into the French zone.

THE CHILDREN'S RATIONS

On the whole the children have received a generous share of the tremendous amount of food imported into the zones. When supplies have been short, it has usually been the policy to meet the children's rations and workers' supplements first out of available stocks; whatever then remains has been distributed on the basic adult ration to the "normal consumers," of whom there are about 10,000,000 in British-U.S. zones who receive no additional supplementary rations of any kind.

The foodstuffs actually provided as rations to children in British-U.S. zones in May, 1948, are shown in the accompanying table. These rations have undergone very little change in the past two years. It will be noted that though these rations provide extremely little meat and fat they at least provide a good amount of milk for the younger children.

Milk.—Supplies have fallen off by about 30% since 1939–43. This is mainly because the German cow is producing very much less milk through lack of imported cattle-feed and because of the poor fodder crop of 1947. It is greatly to the credit of those responsible for the organisation of food distribution in Germany that the limited supplies of milk available have been successfully applied to the needs of young children. Inevitably, however, the older children have received less than their needs. Another unfortunate circumstance is that bad transport and cooling facilities lead to the distribution of much half-sour milk, especially in summer. In some places this undoubtedly contributes to the infant mortality.

Food in Addition to the Rations.—From the table it will be seen that, though the caloric value of the ration for children under the age of 3 years is adequate for their needs, above this age the ration becomes increasingly insufficient to meet energy requirements. For the older children especially, their health and nutritional state depend vitally on food obtained in addition to the rations. The sources of such additional food are as follows:

OFFICIAL MONTHLY RATION ALLOWANCES FOR CHILDREN IN COMBINED BRITISH-U.S. ZONES, MAY, 1948

Commodities (g.)	Age-groups (years)			
	Under 1	1–3	3–6	6–20
Bread	2200	3250	6600	11,000
Cereal products	2175	1500	1250	1100
Potatoes	4500	4500	9000	9000
Fat	375	330	330	330
Sugar	1375	1000	1000	1500
Meat	—	100	100	100
Cheese	—	—	62	62
Milk (skimmed)	—	—	—	6000
Milk (full)	22,500	22,500	15,000	—
Fish	—	—	600	600
Eggs (number)	5	5	5	5
Dried fruit	—	500	500	1000
Calories per head daily	1205	1202	1443	1695

School Feeding.—A school-feeding programme was begun first in the British zone and extended, in 1947, to the U.S. zone, following the recommendations of Mr. Herbert Hoover. In May, 1948, about 5,000,000 school-children in the two zones were receiving a snack of about 300 calories in school, on average five days a week. This snack generally consisted of a sweet "soup" of cereal and milk powder, or sometimes a salted soup containing meat extract and some fat, often served with a bread roll. The distribution is planned to cover the neediest children and is very well organised. It is universally appreciated by teachers, parents, and the children. In the French zone no similar programme is at present in operation, chiefly owing to shortage of supplies.

* I visited Germany in October, 1947, as a British representative on the Combined United States, British, and French Nutrition Committee, and again in May, 1948, as a member of a mission sent by the United Nations International Children's Emergency Fund to investigate the condition of children in the three western zones of Germany. The views and conclusions expressed here are purely personal and do not necessarily reflect the official views of either of these bodies. The account of the food-supplies is based on conditions existing in May, 1948. I understand that the situation has considerably improved since then; the basic adult ration has been increased and more food is appearing on the open market as a result of the currency reform.

Digitized by Google

Relief by Voluntary Agencies.—In May, 1948, voluntary agencies were feeding about 220,000 children, mainly under school age, in the British-U.S. zones. In most cases, however, such supplements have been distributed for a few weeks at most to a given group of children and then diverted to another group, to "spread" a limited number of rations as widely as possible. In a similar manner about 10,000 children in the French zone were receiving in rotation a small number of rations that probably did not exceed 3000 rations on any one day. In addition a considerable number of parcels sent by private persons abroad have been coming into Germany. It is impossible to obtain an over-all estimate of their numbers and the amount of food they contain.

Extra Rations for the Ill and Underweight.—The rationing system in all three zones provides for supplementary rations on medical certification to sick patients and those more than 20% underweight. In the British-U.S. zones the "underweight" ration is for 645 calories daily. The number of persons receiving such supplements varies very much from one locality to another, depending probably on the readiness of local doctors to grant certificates. In the Ruhr district, for instance, the number of the population receiving these supplements is 10% in some towns and over 20% in others where health conditions are apparently no different. These extra rations probably go more often to adults than to children. Direct personal inquiry in various schools generally revealed that the few children who were receiving the "underweight" ration were obviously in need of it. Very often there were others who also appeared in need of extra feeding but had not been certified for it.

Unrationed Food.—In the small towns and villages allotments and gardens are unquestionably of considerable assistance, particularly in the summer and autumn; but in the large bombed cities the number of privately cultivated plots is so few that it is doubtful whether they make any significant difference to the total food-supplies of the people in these cities.

Black Market.—The real extent of the black market is a favourite subject for speculation. It is obviously operated erratically and most unevenly through the population. There is certainly a small group of shrewd and successful traders in black-market food and still a few people with non-essential household property to barter, but most of the working population have no such advantages.

Certain factories have been paying their workers partly in kind, anything from clocks to slide-rules, but it takes time and trouble to trade these for food. More usually the trading is a simple exchange of labour for food. The five-day working week allows the worker to spend one day a week in the country working for a farmer for the price of a good meal and perhaps a few pounds of potatoes and vegetables; but in the neighbourhood of the large cities the price of such labour is cheap and the reward correspondingly small.

For these reasons any estimate of the average number of calories received from black-market sources per head of the urban population must be interpreted cautiously. It is liable to give an erroneous impression of a smooth and efficient distribution, benefiting all classes equally.

German authorities quote a figure between 200 and 300 calories as the average per-caput daily consumption of black-market food. Comparison between the official rations and the actual state of nutritional health of the people might suggest a figure nearer 500 calories, but whatever the true figure it probably declined in the first half of the year with the exhaustion of illegal holdings of potatoes. As one German professor put it, the only generalisation that one can make about the black market is that the most dishonest fare best.

Share in Parents' Rations.—Everywhere in Germany one hears the story that parents, especially mothers, give part of their rations to the children. Since workers and heavy workers receive substantial additions to the basic adult ration, their children particularly are likely to benefit. This frustrates the purpose for which the extra rations are granted—to increase industrial production.

The official rations do not provide sufficient calories for children, except those under the age of 3 years. Every child must therefore receive some additional food from one or more of the sources mentioned above. The diversity of these sources makes it impossible to estimate accurately the average food intake of German children either in terms of calories or of specific nutrients. The best clue to their state of nutrition must come from the medical evidence.

RELEVANT VITAL STATISTICS

Infant Mortality

Official notifications of infantile deaths in the three western zones have been as follows:

		Deaths in the first year per 1000 live births
1938	All Germany (1937 boundaries)	59·8
1946	U.S. zone	95·1
	British zone	107·0
	French zone	88·8
1947	U.S. zone	84·8
	British zone	81·0
	French zone	89·0

Though the general tendency, at least in the U.S. and British zones, is towards a reduction in infantile mortality, the rates are still more than a third above pre-war levels. This is mainly because of the continued high mortality in some of the large bombed cities; for instance, in Mannheim and Ulm (U.S. zone) and in some of the Ruhr towns (British zone) rates of over 100 were recorded for 1947.

Tuberculosis

No separate figures are available to indicate the incidence of tuberculosis among children, but the statistics covering all age-groups may be taken as an index of the general trend. The mortality from all forms of tuberculosis has been as follows:

		Deaths per 100,000 population
1938	All Germany	62
1946	U.S. zone	57
	British zone	63
	French zone	65
1947	U.S. zone	55
	British zone	64
	French zone	65

In contrast to the mortality figures, the notifications of new cases are considerably above the pre-war figures and continue to rise. However, as explained elsewhere,[1] there is reason to think that this is largely a paper increase.

Several professors of pædiatrics, with whom conversations were held, thought that they were seeing rather more cases of tuberculosis in their hospital practices than formerly. It is therefore possible that there is some increase in new cases of tuberculosis among children, though not to the extent that recent tuberculosis notifications seem to indicate.

German public-health officers often emphasise that adult forms of tuberculosis are now commonly seen among children, but it is difficult to find any definite factual basis for this contention.

Other Infections

The incidence of other notifiable infectious diseases is not remarkable and is similar to what might be expected in any European industrialised community. One non-notifiable condition that now seems to be particularly common among children in some urban areas is infestation by worms, chiefly oxyuris, but ascaris also is said to be prevalent.

ANTHROPOMETRIC DATA

Any important incidence of underfeeding (simple calorie deficiency) would be expected to lead to retarded growth, which should be reflected in the statistics for heights and weights of children.

1. Tuberculosis in the British Zone of Germany, with a Section on Berlin. Report of an Inquiry made in September-October, 1947. H.M. Stationery Office. 1948.

Digitized by Google

Very extensive data are available on the average heights and weights of school-children in the three zones during the post-war period. In the U.S. zone 1,850,000 school-children were measured in March, 1948, and comparable data are available from December, 1946, and January, 1948. In the British zone monthly measurements of over 10,000 children have been carried out since December, 1946. In the French zone heights and weights of about 370,000 children have been recorded quarterly. These data show some apparent general improvement in both average height and weight over the past year among children in the British and French zones, and some slight improvement in weight, without much change in height, in the U.S. zone. Children in the U.S. zone are, on average, somewhat taller and heavier than in the British zone, possibly owing to hereditary differences.

It is much to be hoped that this large accumulation of data will ultimately be analysed by some competent authority and published with proper interpretations. For the present, however, it seems dangerous to attempt any interpretation without careful analysis, particularly to attempt any comparison with various standard "norms" for heights and weights at different ages. It would be necessary to take into account the age at which German children should normally reach puberty, with its pronounced effect on the pattern of growth. Moreover, it is no simple matter to decide what the present average stature of an adequately nourished German child should be at any particular age, bearing in mind the general tendency of Europeans to grow with increasing rapidity during the present century. Rather than attempt any immediate conclusions from these anthropometric data, it seems wiser to rely on the clinical appearance of the children as they are there to be seen.

CLINICAL OBSERVATIONS

About 1600 children in the three zones were personally examined by me in October, 1947, and about 1500 in May, 1948. The towns visited, the approximate number of children examined, and the kind of institutions in which they were seen were as follows:

October, 1947

British zone: Hamburg, Hanover, Essen, Düsseldorf. 400 children in 3 schools, a kindergarten, a factory (apprentices), and a nutrition-survey clinic.

U.S. zone: Stuttgart, Nuremberg, Frankfurt. 400 children in 5 schools and a nutrition-survey clinic.

French zone: Trier, Ludwigshafen, Freiburg. 800 children in 6 schools, an orphanage, a gymnasium, and 3 factories (apprentices).

May, 1948

U.S. zone: Wiesbaden, Kastel, Aschaffenburg, Mannheim, Heidelberg. 700 children in 4 schools, 2 kindergartens, a hospital, and 2 nutrition-survey clinics.

British zone: Bonn, Duisburg, Haagen, Dortmund, Düsseldorf. 600 children in 4 schools, 2 kindergartens, 2 orphanages, and a hospital.

French zone: Mainz. 200 children in a school and an orphanage.

This clinical study was deliberately limited to the larger towns, most of which are partly destroyed, because all available evidence goes to show that the serious nutritional problems are practically confined to such towns. Information on food-supplies, vital statistics, the opinion of military-government officers and of German public-health officials, and personal observation during many journeys through the country make it virtually certain that there are no nutritional problems among the "self-suppliers" and "part-self-suppliers" who live in the country and comprise about a quarter of the present population of the British-U.S. zones.

It is reasonably certain that the children here described include a good proportion of those in the worst condition to be found in each of the three zones. In many instances the children for examination were selected by German officials. Inquiry was often made into the basis of this selection, and, on the whole, satisfactory assurances were obtained that a representative sample of children was seen in each locality.

Evidence of Underfeeding (Calorie Deficiency)

Most of the school-children present the appearance of normal health and, undressed, seem in fairly good condition though occasionally hollow-eyed or a little thin, and sometimes with protuberant abdomen, stooped shoulders, and prominent shoulder blades. The girls generally appear in better condition than the boys, and children aged 12–14 better than those 6–8 years. The best-nourished fall into the category of averagely nourished children.

In the British zone, where school meals have been in operation for two years, the distinct impression was gained that the general average of nutrition was more uniform than in the U.S. zone. In the French zone the difference between the best and worst children seemed more pronounced than in the other two zones.

Though the physical appearance of the majority was fairly satisfactory in every school visited, a minority, amounting generally to about 10% but in one school (Kostheim, U.S. zone) involving about a third of the children, were clearly undernourished. The common appearance of these children was that of being undersized, listless, flabby, pot-bellied, and pale. Direct questioning of children presenting this appearance almost always showed that they came from one of the following "vulnerable groups":

(1) Refugees.
(2) Families where the father was absent or dead.
(3) Families who had lost their possessions by bombing.
(4) Large families.
(5) Families with sick parents.
(6) "Problem" families in the social-work sense.

Most of these receive few of the indirect benefits enjoyed by children of established industrial workers, who receive extra workers' rations and part payment in factory products. The condition of children from these vulnerable groups is not revealed in the general statistics, by reason of the better condition of the great majority of school-children.

Pre-school children mostly appeared adequately nourished, only a few being unduly thin.

Adolescents aged 14–18, as seen in secondary schools, were generally in better condition than younger children, probably at least partly for the reason that they came from families in better economic circumstances. In industrial schools, on the other hand, where the lower-income groups were mostly found, there was considerable variation in height, weight, and general condition, and in this group individual cases of definite chronic undernutrition were evident.

Psychological Effects of Underfeeding

Personal impressions were heard from doctors, teachers, and military-government officials about the present psychological reactions of school-children. A common opinion was that, though initial attention in schools was good, children seemed to have difficulty in memorising facts. Many seemed unable to stay awake or to pay attention for the whole period. Emotional instability, especially among older children, was mentioned more than once. Such troubles were said to have notably diminished since school feeding has been established. It is difficult to evaluate these impressions objectively, but nevertheless they are an indication of psychological damage resulting from many adverse environmental factors, including underfeeding.

Deficiencies of Specific Nutrients

Vitamin D.—There is a significant incidence of rickets among infants in the cities. Possibly 1 in every

Digitized by Google

10 infants on average would show three or more of the clinical signs of rickets. In some places the incidence is certainly higher; for instance, in Mannheim (U.S. zone) the infants of a random sample of the population, seen by me, were in particularly poor condition; almost all had rickets, and some were marasmic. This city has an unusually high infant mortality, which is probably due to two causes: the disorganisation of its milk-supply, and the large number of families still living in the basements of wrecked houses. Synthetic vitamin D ('Vigantol') is manufactured in Germany, but its distribution for the prevention of rickets is not always satisfactory.

Vitamin A.—There is a theoretical possibility that vitamin-A deficiency might arise through a lack of sufficient fat in the diet to facilitate the absorption of carotene. However, there appears to be no objective evidence of such deficiency among the children. Slight degrees of follicular hyperkeratosis are fairly frequent, as in British children, but it is reasonably certain that vitamin-A deficiency is not the only cause of this condition. No complaints were made of poor night vision (hemeralopia) among children.

Vitamin-B Complex.—There is no clinical evidence of deficiency of any component of the vitamin-B complex, except possibly riboflavine. This is scarcely surprising in view of the good amounts of the complex that must be provided by the high-extraction cereals now commonly consumed. An occasional case of very mild angular stomatitis may be encountered, doubtfully due to riboflavine deficiency.

Vitamin C.—Among the children examined in October, 1947, the incidence of gingivitis was rare. A quite different impression was gained in May, 1948; in some localities inflamed gums seemed to be unusually common among the children; further, out of 1500 children seen 3 cases were discovered in which the gums present the swollen livid hæmorrhagic appearance of clinical scurvy. In several other cases the gums were unusually swollen though no longer acutely inflamed, suggesting partial healing of scorbutic changes. By May, 1948, when the second survey was made, some green vegetables had already been distributed in most localities. The impression was gained that, had the survey been conducted a month earlier, more scorbutic gingivitis would have been seen.

Fruit and green vegetables were extremely scarce in the large cities during the past winter; moreover, the partial failure of last year's potato crop was a further limitation to the supply of vitamin C. It is difficult to avoid the conclusion that there has been a significant incidence of vitamin-C deficiency among children during the spring of this year.

Protein.—Famine œdema has been a popular clinical diagnosis in Germany during the post-war period, as is usually the case in a country short of food and under military occupation. However, in the course of four tours carried out by me in the past three years, and covering 25 large towns in western Germany, not a single case of undoubted famine œdema, due primarily to lack of food-supplies, has been seen either among children or adults; this despite the fact that the German public-health authorities were often responsible for selecting the subjects examined and had opportunities to produce their cases, if any existed. The last undoubted cases of famine œdema seen by me were at Belsen concentration camp.

Serum-protein determinations have been carried out among samples of the child population in the British and U.S. zones in recent months. It is to be hoped that the results of these surveys will ultimately be published. Without wishing to anticipate their publication, I may say that the results give no grounds for anxiety.

The present extreme shortage of animal protein in the common diet tends to be emphasised by the German public-health authorities as a matter of physiological importance. But there is good reason to think that the mixture of amino-acids from various vegetable sources, together with the amount of milk regularly provided by the ration, are sufficient at least to prevent any serious protein deficiency among children. There can be no question, however, that the present supply of milk and other sources of animal protein generally falls far short of a level that could be considered ideal and, moreover, is much below the level to which the Germans have been accustomed.

Fats.—Fat is valuable as an article of diet because it is a concentrated source of calories and has a high satiety value. Moreover it is extremely useful for cooking and for making the diet appetising. Nevertheless there is no good reason for believing that lack of fats is leading to any serious physical damage to children in Germany.

Iron and Calcium.—The results of hæmoglobin determinations carried out on children in the British and U.S. zones were kindly made available for inspection by the British and American public-health authorities. From the figures submitted I am satisfied that there is no important incidence of disabling anæmia among the children. Individual cases of pallor suggesting anæmia were encountered in the course of examining children, and it is concluded that there is probably a small incidence of moderate anæmia, probably due to iron deficiency, among the city children.

There is no simple clinical way of deciding whether lack of calcium is a limiting factor to the growth and development of German children. Milk, the most important dietary source, is provided in good amounts for the youngest children, but for the adolescents, especially, supplies are seriously below desirable levels. In the British zone the supply of calcium is improved by the addition of calcium carbonate to the bread, as is the practice in Great Britain.

Iodine.—Simple goitre is common among the children in the southern part of the French zone and some parts of the American zone. These have always been centres of endemic goitre. There appears to be no definite evidence whether the incidence has altered as a result of the post-war food restrictions. Lack of iodine is probably the primary cause, though other factors, such as the consumption of certain vegetables, may play some part.

Dry Skin.—Several cases of unusually dry desquamating skin were observed in almost every group of children examined. The incidence appeared to be higher than could be considered normal. However, there is no certainty that this can be considered a sign of nutritional deficiency; lack of soap may be an important contributory factor. In view of this lack it is remarkable how clean and healthy the skin appears in the great majority of children.

ENVIRONMENT AND MENTAL HEALTH

Though the state of physical health and nutrition of the great majority of city children is thus relatively satisfactory, one cannot feel the same about their mental health. Their daily life is passed in an environment that presents many bad sociological and psychological influences, tending to encourage insecurity and frustration, with the danger of consequent aggressive compensations.

Overcrowding.—Most of the large cities in western Germany are 20–80% destroyed. Something of the vastness of the problem may be gathered from the calculations of a Hamburg architect that there are, in the whole of Germany, more than 520,000,000 tons of rubble still to be cleared. Probably 1 room in 4 has been destroyed. In addition, from the influx of refugee Germans 1 person has been added to each 4 who must be housed. Nevertheless, except for the miners, no significant

Digitized by Google

advance seems to have been made in the supply of city dwellings. Often the only notable building activity is the re-roofing of a church or the repair of an ancient monument.

Fuel.—Domestic fuel has been short everywhere since the woodwork torn from bombed buildings was used up. In winter the poor have had to make the most of their little fuel by heating one room, crowding into it, and not ventilating it lest the heat escape.

Clothing.—German children still living in their own homes were comparatively very well clothed at the end of the war. At least a fourth of the population, however, were bombed out at least once and lost much of their clothing. In addition, a sixth of the present population of British-U.S. zones came in as refugees, usually with only the possessions they could carry. As a result nearly half of the population are in definite need of clothing. Even the rest are rapidly running out of shoe-leather and garments made of cotton. A small but important matter has been the extreme shortage of sewing-thread, which commands fantastic prices in the black market.

Soap.—The current soap ration provides every person each month with a tablet of soap about a fourth the size of an ordinary cake of toilet soap, just enough to wash a child all over with soap once a week. Some families get extra soap in parcels from abroad or as part of the father's wages if he works in the right factory. In addition, a small amount of detergents is available for the washing of clothes. Few homes can provide any hot water for washing. In the circumstances, especially in the midst of all the dust and dirt that surround everyone in a bombed city, it is amazing to see how clean the children are kept. Relatively few city children are dirty, except for their bare feet.

Food.—Whatever may be said about the nutritive value of the present diet, it is certainly extremely monotonous. The average German child is fairly happy with a diet of bread and potatoes, provided there is some fat and a bit of meat to go with it. But the perpetual bread and water-soaked vegetables of the present diet, even though tolerable to the healthy child, are certainly not stimulating to the child with a fickle appetite.

Home life has been generally disorganised. At least half the people in the cities in Western Germany have had to move from their normal homes, either because of bombing or because they are refugees. They are living with relations or have strangers billeted on them. Hundreds of thousands are still living in the basements of their wrecked homes. Since work must be found wherever factories are standing, the breadwinners are often forced to live away from home. As in many other countries, families were split up during the war, and the years of separation have been prolonged for the German families in which the fathers have been held as prisoners-of-war. An astonishing number of children still say that their fathers "have not come home from the war."

Black Market.—Most of the children are exposed every day to constant discussions within the family about how tomorrow's inadequate rations can be increased through the black market. Every member of the family must do what is necessary, and it is said that many well-brought-up children have been stealing food to help their families.

Schools.—Almost all the school buildings are dirty, cold, damp, and often partly destroyed. Two or even three separate schools use the same class-rooms, working in shifts so that school hours are shorter than normal. Paper, books, and writing materials are still extremely scarce. The teachers are shabby and underpaid; they look tired and are often dispirited. Too many of them are elderly. One gathers the impression that, to maintain discipline in large classes (which sometimes contain up to 75 pupils), they rely too much on the system of stern orders and immediate obedience—the system under which they themselves grew up. Though much effort has been expended by the occupying authorities to revive in the universities true scholarship, which the Nazis suppressed, this is necessarily a long-term project from which, as yet, the city children show little signs of benefiting.

Isolation.—The older children especially seem to share with their parents the feeling of isolation from the outside world and indifference to events taking place in it. Distribution of newsprint is limited, wireless sets are often worn out, and there are almost no posters except those chalked on walls by political propagandists. The former intellectual isolation of Germany, so well described by Thomas Mann,[2] is doubly intensified now and, for the moment, the people seem emotionally exhausted.

DISCUSSION

Life in the bombed German cities has been both physically disagreeable and psychologically disheartening during the past three years. The reaction of the people to their consequent misery has been to focus their complaints on the one thing that they see clearly—the obvious inadequacy of the official rations. Perhaps partly because of this constant insistence on food, a tremendous effort has been made by the occupying authorities to keep the people fed by means of imports; in fact, about two-thirds of the bread distributed in Western Germany during the past two years has been made from imported grain. As a result, the children have been saved from starvation and even from serious underfeeding and malnutrition. But no similar effort has been concentrated on the other influences that make life in the bombed cities miserable: gross overcrowding, lack of warmth, worn-out clothing, lack of washing facilities, disrupted home life, the immoral pressure of the black market, and, perhaps most important for the future, the lack of proper education.

The overwhelming impression of a physician visiting Germany is the dangerous social and psychological environment in which the children of the bombed cities are growing up. By comparison with this, their nutritional health is now a minor issue.

SUMMARY

A brief account is given of the child population of Western Germany and the sources of its food.

The relevant vital statistics are considered.

Observations are presented based on the personal examination of over 3000 children seen on two recent visits to Germany.

It is concluded that, though the general level of health and nutrition among the great majority of children in bombed cities is relatively satisfactory, there is a minority, comprising the "vulnerable groups," whose physical condition is poor.

It is emphasised that, by comparison with their nutritional health, the social and psychological condition of the children is likely to be a much more serious issue.

Grateful acknowledgment is made to the numerous officials of the occupying governments, German public-health officials, doctors, teachers, parents, and children who supplied the information that provides the background of this paper.

In particular I wish to thank the following senior officers for their very great assistance on both visits to Germany: Colonel Milford T. Kubin, public-health branch, O.M.G. (U.S.), Brigadier W. Strelley Martin, M.C., chief, public-health branch, C.C.G. (British), and Médecin Général G. Coulon, directeur de la santé publique, G.M. de la zone Française.

I also wish to thank my colleagues on the UNICEF Mission: Mr. S. M. Keeny, recently chief of the UNRRA Mission to Italy, and Dr. C. E. Raiha, deputy chief, University Pædiatric Clinic, Helsinki, Finland. I have drawn freely on their ideas and observations, but they do not necessarily agree with the interpretations given in this paper.

2. Mann, T. *Yale Rev.* 1946, 35, 223.

Digitized by Google

MEDICAL RESEARCH IN AFRICA

FROM A CORRESPONDENT

Now that it is at last agreed that the only hope of avoiding world starvation lies in the immediate and full development of the food-producing potentialities of tropical Africa, it is evident that medical, veterinary, and agricultural research assumes, to use a popular war-time phrase, "top priority." Officially, this is said to be an accomplished fact, but a recent tour of East, Central, and South Africa raises doubt as to whether the true urgency of the position is appreciated in Whitehall and whether the matter is being tackled in the right manner. The following comments and criticisms apply primarily to the medical aspects.

The urgency has been made abundantly clear by the writings and speeches of such international experts as Sir John Boyd Orr and Sir Jack Drummond. What is not so generally appreciated is the nature and the size of the medical problems involved. If the full food-producing potentialities of tropical Africa are to be realised, it is essential that the physical capacity of the native should be developed to the fullest possible extent. From the medical point of view this involves improving the nutritional status of the native and controlling the diseases to which he is subject—two subjects on which we are still very much in the dark. Through no fault of the members of the Colonial Medical Service, but simply because the men and the money have never been forthcoming, there is still relatively little information about such elementary data as the incidence of disease in different colonies and protectorates. For instance, the full geographical extent of the yellow-fever virus is still unknown. The evidence for the incidence of leprosy in East Africa is entirely inadequate and the first systematic survey of the extent of this disease in East Africa is only now being carried out. Again, there have never been any facilities for carrying out controlled clinical trials of new therapeutic agents there. Anyone with even a superficial knowledge of tropical medical literature must have been impressed with the number of published articles based upon the clinical trial of a new preparation in only 50–100 cases, though thousands (if not hundreds of thousands) might have been investigated if only the Colonial Office had made it possible. Closely interrelated with this question is that of the varying reaction of a disease to a given drug in different parts of the world—even in different parts of the same continent. Kala-azar is a case in point, as are the contradictory reports now being received about the efficacy of 'Paludrine.'

As regards the nutritional status of the native, scientific data are again lacking. Surveys have been made but with one or two notable and oft-quoted exceptions they have merely touched the fringe of the problem. Even those which have been made are partially invalidated by the unfortunate fact that we are still hopelessly ignorant of the physiology and the feeding habits of the normal native. The result has been that socially minded publicists have been making statements about the nutritional status of the native for which there is no scientific basis. For instance, what scientific reason have we for declaring, as is sometimes done (and regrettably, let it be added, by some who have allowed political bias to impinge upon scientific reasoning), that the nutritional requirements of the African native are the same as those of Europeans? Or, to take a more specific instance, assuming for the moment (and it is only an assumption) that the calorific requirements of, say, an 80-kg. native doing a given piece of work are the same as those of an 80-kg. white man, what evidence is there that the native requires the same proportion of carbohydrate, fat, protein, and vitamins as the white man?

THREE MAJOR RESEARCH PROBLEMS

To indicate the problems involved, even in such bare outline, is sufficient to emphasise their tremendous scope, and it is clear that fundamentally there are three major research problems which, though closely interlinked, must be considered separately to avoid making confusion worse confounded.

First, we must acquire more data on the normal physiology of the native and his nutritional status. What are his "normal" height and weight? Are his pulse-rate and blood-pressure the same as those of Europeans? Are there any differences between his metabolic processes and those of a white man? What is his normal reaction to physical exertion and to emotional stress and strain? What is his physical stamina? What are his normal requirements of sleep? Until we have at least some elementary data on such basic matters, it is impossible to evolve any long-term policy for his betterment.

Secondly, surveys must be made on the incidence of disease in different areas. How widespread is tuberculosis, and what form does it tend to take in the native? How widespread is schistosomiasis? What is the real incidence of relapsing fever, and what are the real relationships between the louse-borne and the tick-borne varieties? Closely linked with this subject is that of vital statistics. What is the expectation of life in the native? What are the infant and maternal mortality-rates—not in areas covered by hospitals and clinics but in the whole colony concerned?

Finally, there is the problem that the mere mention of tropical medical research usually suggests—the means of treating such classical diseases as leprosy, malaria, schistosomiasis, and trypanosomiasis. Here much has been accomplished, but much more requires to be done, particularly in ensuring that trials of new remedies are carried out on a sufficiently large scale and with enough controls to make the results capable of statistical analysis.

TWO DANGERS

Two unfortunate tendencies are appearing in the plans to cope with research. It is probably true to say that the Colonial Office has accepted the principle that medical research in the colonies is a matter of some urgency; but unfortunately, as all too many of us are learning from bitter personal experience, the time-lag in governmental quarters between acceptance and action is liable to be all too long. What is much more disturbing, however, is the evidence that the action that is being taken is along the wrong lines.

Remote Control from Whitehall

The first danger is that too much control is being exerted from Whitehall, and that insufficient attention is being given to the views of those with years of experience in the colonies. Fundamentally, the approach to research is the same the world (and science) over, and no-one would dream of questioning the advisability of obtaining advice from experienced research-workers and administrators in chemistry, bacteriology, nutrition, pharmacology, and medicine. But advice is a very different matter from direction, and you cannot direct research in Africa from an office in Whitehall or an armchair in the Athenæum. Neither can you send a bright young research-worker from this country out to Africa and expect him to do good work until he has had actual experience of the conditions under which he has to work.

Quite frankly, and for the sake of Africa frankness is now essential, the workers in the field are becoming tired of the continual stream of "experts" being flown out to them for brief tours by the Colonial Office, without any definite action being taken as a result of their reports. They are resenting even more what they

Digitized by Google

consider to be the dictatorial methods being adopted by the higher level of bureaucrats both in the research and the administrative sphere. They are delighted to have visitors from the United Kingdom. No-one is keener than they that research work should be expanded, but they cannot understand why their opinions are so steadily ignored—or at least so it appears to them.

What is even more disturbing is the suggestion that a young man can start doing sound research the moment he arrives in a colony. This is fundamentally wrong, except in the case of the basic sciences such as chemistry and physics. And Africa is not the place for such basic work to be done. The United Kingdom, with its well-equipped research institutes, whether university, government, or industrial, is the place for such fundamental work to be carried out. It is only as the stage of field trials, whether laboratory or clinical, is approached that it becomes incumbent for the work to be done on the spot. What does not appear to be appreciated in certain research circles in Great Britain is that no reliable work on medical (and nutritional) problems can be carried out until the persons undertaking it have a sound knowledge of the people on whom it is being done and of their conditions of life.

Coördination of Colonial Medical Service and Colonial Medical Research Service

The second danger is the lack of coördination between the Colonial Medical Service (C.M.S.) and the new Colonial Medical Research Service (C.M.R.S.). In these days of the glorification (some would say almost the deification) of research, there is a very real danger of all the most promising and outstanding of recruits for the C.M.S. being recruited for the C.M.R.S. and, in due course, receiving all the plums of the service in the way of accelerated promotion and the better-paid appointments. The effect of this policy on the C.M.S. would be disastrous. Any able young doctor proposing to work in the colonies would immediately go for the C.M.R.S. because of the better prospects, thus leaving only the mediocre ones for the C.M.S.

What is required is that, except in special cases, recruitment in the first instance should be primarily to the C.M.S. After a preliminary period of, say, two years, transfer to the C.M.R.S. should be considered if the doctor has shown any special aptitude for research. This transfer should never be automatically permanent, and ample opportunity should be allowed for interchange between the two services. Conditions of service should be the same in both, and there should be equal opportunities for promotion to the highest levels. In this way the standards of both services would be raised, and there would be no opportunity of the health services of the colony suffering because of the brains all being concentrated on the research side. After all, a sense of proportion must be maintained, and research-workers must never forget that, so far as medicine is concerned, research is the handmaiden of the practising doctor.

SOME PRACTICAL SUGGESTIONS

The critic should always try to be constructive lest he be dismissed as being merely destructive. Let me attempt a bare outline of how the Colonial Medical Services should develop.

Conditions of service must be improved immediately; and, in view of the developments in this country under the National Health Service Act, the salaries to be paid under the new scheme must be taken as the basis for salaries in the colonies. Unless the financial attractions of the colonial services are as great as those in Great Britain, the right type of man will never be obtained. A scheme must be evolved whereby there will be full interchange between the higher ranks in the clinical side in the colonies and in the United Kingdom. For instance, those of registrar status in the United Kingdom should be encouraged to accept positions as consultants in the colonial service for a period, on the strict understanding that by so doing they will lose neither in seniority nor in superannuation rights, should they ultimately decide to return to service in Great Britain. Similarly, promising men of consultant status in the colonies should be encouraged to spend periods of, say, two or three years working in this country, again with no loss of seniority or superannuation rights. This was a point which was emphasised, particularly in connexion with the new medical schools in the African colonies, by the late Professor McSwiney, whose outstanding report on the subject appears to have been permanently lost in one of the many pigeon-holes of the Colonial Office.

On the research side, as already mentioned, the new Colonial Medical Research Service must be closely linked with the Colonial Medical Service. As in the case of the C.M.S., there should be a close association with research-workers in the United Kingdom, both as regards personnel and as regards the work. For instance, it would be a waste of time, money, and man-power to build and equip elaborate research laboratories and institutes in the colonies: the fundamental work in biochemistry, pharmacology, physics, and the like can all be done much better in research institutes in the United Kingdom, provided there is close collaboration with the men in the field—i.e., the workers in the colonies must be consulted about the work to be done, kept in close touch with the progress of the work, and allowed to spend spells in the laboratories in the United Kingdom when necessary. Conversely, the chemists and the laboratory workers in the United Kingdom must visit the colonies at regular intervals so as to be able to appreciate the full implications of the work in which they are participating.

In all these matters the fullest consultation must be maintained with the men in the field. As already pointed out, the present tendency to ignore the men with most practical experience of tropical medicine is not only alienating the members of the Colonial Medical Service but is also tending to the preparation of plans which have little hope of success.

In spite of all that has been said about the necessity for research on such fundamental questions as the incidence of disease and malnutrition, this does not mean that there are no short-term problems to be tackled immediately. Even though we are so ignorant about the nutritional status of the native, there are areas where gross malnutrition undoubtedly exists. Then there are the vital problems of the control of the tsetse fly, the treatment of trypanosomiasis, the use of insecticides such as D.D.T., and the control of helminthiasis. All these can be tackled in a practical manner pari passu with the inauguration of the more elaborate research programmes.

All this will require more men and money, and much more money than the Treasury will concede except under greater compulsion than has so far been exerted. This is not the place to argue the point; but, if it is conceded that the only hope of avoiding world starvation is the full development of tropical Africa, and that this development depends for its success on raising the physical status of the natives and making life there healthier for white men, even the Treasury will find it hard to enforce its conventional obstruction to the necessary expenditure.

But, above all, what is required now is direct access of the C.M.S. and the C.M.R.S. to the Secretary of State. Much lip service has been paid of recent years to the development of the colonies. On the medical side little of practical value has resulted, and it is clear that one reason for this is that the medical services

Digitized by Google

have not had the direct access to the Secretary of State that is essential. One way in which this could be accomplished would be by immediately increasing the seniority of the office of medical adviser to the Minister —if necessary, to that of an assistant secretary of State— so that he would have the direct access which is necessary. If this is done, it is equally essential that the occupant of the post should be a doctor of outstanding ability, both medically and administratively. At the present stage much could be said for appointing him from outside the Colonial Medical Service. Men of the calibre of the late Professor McSwiney, with his unusual combination of outstanding ability in the spheres of medicine, research, administration, and medical education, may unfortunately be rare, but it is such a man who is required at the moment to undertake the reorganisation of the Colonial Medical Service and to ensure that his reforms are transmitted personally to the Secretary of State for immediate action.

W.H.O. CONFERENCE ON STREPTOMYCIN

AT the third session of the Interim Commission of the World Health Organisation, at Geneva, in April, 1947, it was resolved to set up an expert committee on tuberculosis. In the first report of the committee,[1] accepted by the Interim Commission, the various field activities and techniques for tuberculosis control were set out and it was stated that the best contribution which W.H.O. can make to tuberculosis research would be in developing and recommending uniform procedures. Special problems would require the services of subcommittees who were expert in highly specialised fields. Among the most urgent of these problems was the evaluation of new chemotherapeutic agents such as streptomycin, and accordingly a conference on streptomycin therapy in tuberculosis was convened in New York on July 30 and 31. The following experts attended: Prof. K. Choremis (Greece), Prof. C. Cocchi (Italy), Dr. Robert Cruickshank and Dr. M. Daniels (United Kingdom), Prof. R. Debré (France), Prof. R. Dubois (Belgium), Dr. H. Corwin Hinshaw and Dr. H. McLeod Riggins (U.S.A.), with Dr. H. E. Hilleboe (U.S.A.), a member of the parent committee, as chairman. In addition, American experts in different fields of streptomycin therapy and in the pathology and bacteriology of tuberculosis were invited to attend the meetings.

In the first three sessions the discussions covered the general principles of chemotherapy in tuberculosis, the results obtained with streptomycin in different forms of tuberculous infection, studies in combined chemotherapy, and laboratory methods for the diagnosis of tuberculosis and for the control of streptomycin therapy. A strong impression from the reports of members from some European countries was that acute tuberculosis in childhood (tuberculous meningitis and miliary tuberculosis) was much more common there than it is in the U.S.A., and that results with streptomycin in these acute childhood infections were more encouraging than earlier reports had suggested. The present position in the chemotherapy of pulmonary and surgical tuberculosis in the U.S.A. was reviewed by Dr. J. Barnwell, of the Veteran's Association, who analysed over 3000 treated cases (shortly to be published); by Dr. Hinshaw, representing the Trudeau Society; and by Dr. Riggins, representing the American Tuberculosis Society; while Dr. Floyd Feldman outlined the trials now being sponsored by the U.S. Public Health Service. The tendency in American centres is to reduce dosage to 1 g. per day (or 20 mg. per kg. body-weight), with a resultant reduction in toxic reactions but with little obvious change in therapeutic effect, and to shorten the duration of treatment to 60, 42, or even 28 days in cases of pulmonary tuberculosis in the hope of preventing or minimising the development of streptomycin-resistant strains of the tubercle bacillus. Remarkable results were reported by Dr. Edith Lincoln in the treatment of small groups of cases of tuberculous meningitis and miliary tuberculosis with streptomycin and 'Promizole' (a sulphone compound), the latter drug being continued for many months after streptomycin therapy was stopped. Dr. Daniels described the organisation, under the ægis of the Medical Research Council, of the streptomycin trials in tuberculous meningitis, miliary tuberculosis, and progressive bilateral pulmonary tuberculosis in Great Britain. Laboratory methods were discussed by Dr. Cruickshank and Mr. W. Steenken, while Dr. R. J. Dubos made a strong plea for discarding "egg-concoctions" in favour of the oleic acid and bovine albumin diagnostic medium for the isolation of the tubercle bacillus.[2]

At the final session, attended only by members of the W.H.O. subcommittee, recommendations were drafted concerning the use and value of streptomycin in tuberculosis. The following points were stressed:

In most forms of tuberculosis streptomycin is at best an adjuvant to other recognised therapies; its use is not devoid of risk of the development of toxic reactions, and, more serious, of streptomycin-resistant tubercle bacilli which may be transmitted to exposed contacts.

The drug should at present be distributed through government or other responsible health agencies to hospitals and institutions where it can be used under expert supervision. Patients with tuberculous meningitis and miliary tuberculosis in whom the use of the drug can be a life-saving procedure should have priority.

In certain other forms of tuberculosis—e.g., acute pulmonary, tracheobronchial, sinuses, and fistulæ—streptomycin, judiciously used, could be a useful adjuvant form of therapy.

Size and duration of dosage could not yet be defined within narrow limits.

The wide variations in methods of reporting the results of streptomycin treatment from different centres made comparisons of the efficacy of different therapies impossible, and the committee urged the adoption of certain minimum standards of reporting which will render such comparisons possible and valid.

W.H.O. should continue to encourage and facilitate international study and coöperation in researches on the chemotherapy of tuberculosis.

The memorandum embodying these recommendations has now been accepted by the tuberculosis expert committee and forwarded for approval to the executive board of W.H.O.

After the conference, the delegates made a weekend outing to the Homer Folks Sanatorium, Oneonta, belonging to the New York State Department of Health, where many clinical and laboratory problems in the streptomycin therapy of tuberculosis were discussed in detail.

1. *Bull. World Hlth Org.* 1948, **1**, 205.

2. *Amer. Rev. Tuberc.* 1947, **56**, 334.

". . . sickness used to arise from too little food. Now it comes from too much worry. Doctors could only alleviate, not cure, the old kind of disease until social conditions were improved. To-day they can only deal with the symptoms of the present diseases, because they cannot produce world stability. Add to this the fact that modern medicine is well on the road to abolishing, or at any rate rendering unimportant, many of the more serious illnesses that used so often to be fatal, like diphtheria and pneumonia, and you see that once again science is giving us the physical tools of mastery, but they are not much use to us because we remain mentally a lot of frightened, irresponsible, and neurotic children."—*New Statesman and Nation*, London Diary, Oct. 9, 1948, p. 297.

Digitized by Google

In England Now

A Running Commentary by Peripatetic Correspondents

TWENTY years, I suppose, is a long life for a dining club; but our members were very carefully chosen—half a dozen men who had been close friends all through their student years picked the rest. So, though what was once a hilarious evening for a bunch of lively young ex-Residents has become a more sober gathering of senior partners, with a sprinkling of specialists and oddments, we still come; and I think the club will survive until we are all dead, bedridden, or too broke to afford the fare up.

None of the members has died yet; 3 (out of 15) have had phthisis and 1 has a colostomy, but they are still ambulant; nor do any look potentially broke—some of us look thin and ill, and most of us look worried, but an outsider would guess we were a pretty successful and prosperous lot of doctors. My own first impression each year, on seeing them gathered round the cocktail table waiting for the gun, is that they have not changed a bit—not in face, or facial expression, or tone of voice, or conversational gambit; only in hair, for all but 2 of us are going grey and 1 is getting a little bald. But if the said outsider was given a flash-back of the club when it was founded he would soon spot the effects of twenty years' battering by night-calls, overdrafts, and the frustrations inseparable from family life.

Much the same applies to our conversation. Though we greet one another in the same words we no longer all speak at once; we listen, if not gravely (that will come in the next twenty years) at least with restraint, to what the other has to say. We were always individualists, but where once our opinions were second-hand (and every member knew whom they came from), now they are based on first-hand experience plus personal prejudice, and are therefore almost unshakable—an effect of twenty years' laying down the law.

Most of us have boys and girls at school, so there was the usual parental false modesty over the children's prowess: "Peter hasn't a hope of getting through Common Entrance . . ."; "Jimmie has been two years at St. Ethelred's and is still bottom of the second form . . ."; that sort of thing, with an occasional casually dropped remark that Peter or Jimmie won the open hundred yards at the age of 12, or topped the batting averages at his prep. school, but what's the use of that? An astonishingly high proportion of us have faced near-tragedy in our wives or children; but of that we did not speak. We don't go in for speeches, thank God, but there were the usual reminiscences, starting with a "Do you remember . . . ?" to one's neighbour and taken up by one after the other across the table. There was that Christmas when our minstrel troop performed at a home for the aged sick. The troop arrived to find the inmates sitting round long tables in the big hall, apparently waiting for our show to start. But half way through the opening chorus it suddenly became clear what they were awaiting—TEA. From the moment when the bread and butter clattered in the audience never looked our way again; and such was the clash of knife and teaspoon that our noisy show was audible only on the stage, if that. Even when our president, slightly tight, came on to announce "the next item is a song by Mr. Robinson," then re-entered to say "Mr. Robinson will now sing *The Blue Room*," and finally came on a third time and burst into song the inmates didn't smile. If our outsider had peeped in while this little story was being pieced together he would have realised that the changes in us since 1928 have been merely organic rather than functional.

* * *

The eminent surgeon on my right looked askance at my broken nails and roughened scratchy hands, while the equally eminent physician on my left watched and wondered why I fumbled with the armament of cutlery. They hadn't a clue—could not guess that throughout the week I had been working at a Volunteer Agricultural Camp, lifting potatoes and picking apples at 1*s.* 7*d.* an hour. As I gobbled the roast turkey I reflected that my previous evening meal had been of meat which might well have functioned in the 1938 Grand National and I had washed up my simple platter and tools in the communal tub of greasy water. What would our scarlet-coated toastmaster have made of that?

From the literature received one fondly imagined one would be accommodated in an ancestral mansion. Alas, B— Hall was a ruin and our lot was cast in huts. But, having made my bed with the four blankets and pillow provided, I for one at the end of the day's work was ready enough to lie in it, however hard it was, and however restless and adenoidal my campmate in the lower berth might be.

Reveille was at six: no bugle note, but shouts of "Wakee-wakee" and thumpings on the hut side. After a very adequate breakfast—the porridge especially was good, though lacking sugar and milk—we went by lorry, car, or bike to our allotted farm, carrying sandwiches whose size was more remarkable than their succulence. "My" farmer had applied for only two volunteers for apple-picking, and my mate was a silent and aloof miss from Surbiton. The fact that it was her second week in camp perhaps accounted for her superiority. We worked from 8 A.M. till 9.30 when there was a short interval for refreshment. At noon we lunched with the other farm-hands in a shed, the farmer providing copious hot sweet tea to combat incipient shock or collapse. Another three hours and we were free to return to camp, feeling we had well earned the 11*s.* 1*d.* that Farmer Giles doled out from a huge wad of notes. Personally I don't think he'd made a bad bargain.

There was a certain fascination in apple-picking—the skilful laying of the ladder to ensure the maximum gathering, the delicate touch to prevent one of a great clutch falling, the satisfaction of lifting three at a time in each hand. Some of the fruit, mostly "Lane's," was magnificent, often scaling well over a pound apiece; and a reddening apple with the dew still on it is a far prettier sight than, shall we say, a gangrenous appendix.

The same cannot be said of spud-lifting, where one is the slave of the inexorable spinner and must follow up one's stint ventre-à-terre, keeping pace with the regulars and locals who are paid considerably more for a day's work, so that one has verily to bear in mind the Parable of the Vineyard. It's a backaching, soul-destroying job; but preferable, as well I know, to sugarbeet lifting or to threshing, especially of beans.

Should this be read by the village doctor who (out of surgery hours) courteously lifted an apple twig from my palpebral conjunctiva, I should like again to express gratitude. It was odd I thought that neither of the two uniformed members of the B.R.C.S. who graced the camp knew how to evert a lid and had been warned by doctors against the attempt. Surely it is the simplest of measures, resulting in immediate and miraculous relief of considerable agony.

To one in search of recreation as opposed to holiday I would recommend a V.A.C. But he, or she, must be a good "mucker-in" and have sturdy digestive and sleeping habits. My camp was clean and well run; the food and showers were hot and much was done for one's entertainment and convenience. For my part, I shall go again and add my drop to the ocean of production; albeit my earnings for a week, by the very sweat of my brow, were equalled almost to a shilling by the cost of my Hospital Dinner (plus wine).

* * *

After recovering from the preliminary shudder set up by your annotation *Patients' Reading* (Oct. 9), one has to admit there may be something in the idea. The shudder was solely in response to the notion of "prescribing books like medicine, and requiring a report from the librarian on the effect on the patient." Just imagine ploughing through the folder of notes, path. forms, blood-counts, X rays, and the rest, so swiftly collected by the modern medical case, and then stumbling on a note: "Will the Librarian please see? P.A.; r.b.c. now 3,500,000. Is he strong enough for James Joyce?" Before long I suppose students will be asked the volumes to prescribe for specific diseases and the textbooks on therapy will note "*Gone With the Wind* is almost specific in this condition" and "Meredith may be exhibited, but must be instantly withdrawn on signs of the patient's weakening."

A librarian's advice would indeed go far to prevent occasional unfortunate selections, instanced by the

Digitized by Google

sufferer from persistent jaundice who chose on too superficial but sympathetic grounds *Forever Amber*, and the G.P.I. who roared his head off all the way through one of Laski's books on Socialism, no less. Then there is the complication first described by P. G. Wodehouse, the physical weight of the tomes offered for recumbent reading. The patient with epigastric tenderness could hardly be expected to stomach Scott; he should be started on Shelley, progressing through Bacon to the Brontës. Digestion of the first three chapters of *Vanity Fair* indicates complete symptomatic relief.

Uncoöperative sufferers on extra fluids will do well on P. C. Wren, or might advantageously have *The Ancient Mariner* recited to them t.d.s. Victims of anorexia nervosa could only thrive on Damon Runyon's *Piece of Pie*, in which a character by the name of Nicely-nicely Jones enjoys an eating competition of toothsomeness more than somewhat. The B.M.R. in thyrotoxicosis can be lowered to normal in a week by *Paradise Lost*, and Gibbon will quieten even acute mania. Anyone with a gastric ulcer should be put to bed with a copy of Lin Yutang's *Importance of Living*, while the essays of Stevenson and Lamb can knock at least 50 mm. Hg off a hypertensive blood-pressure. *Alice in Wonderland*, followed by anything from Chesterton and Belloc, may be reserved for the non-specific restoration to sanity in us all. Pregnancy will pass peacefully with Jane Austen. For general depression how about Leacock, Thurber, Benchley, et al.? For lethargy there is always Peter Cheyney, and insomnia may be instantly relieved by any reputable textbook on hæmatology.

* * *

As usual at this season the winter-pants problem has been causing me concern. Whether to don them as soon as the mornings get chilly and be boiled by midday; or to start work blue and begin to feel about right at lunch-time. This isn't a question on which tradition gives any guidance. Everyone knows that he must ne'er cast a clout till May be out (though there is some disagreement about the capital letter in "May"); but on when to resume the cast clout the wise rhymesters are silent. No-one says:

Don thy woolly smock
As soon as it be Oc.

Or:

When chestnut leaf do fall
Cotton ain't no use at all.

Or even:

Car won't start in the morning
Shepherd's warning.

Clearly it was the chills of late spring, rather than of early autumn, that our ancestors feared. Anyway, since it is looked on as eccentric, even at the peculiar club where I feed, to doff one's underwear in the cloak-room, I support that school which stays in bed till noon and carries on to the bitter end with the summer-weights.

* * *

I find in the *Medical Times* of March 17, 1849, the following "advertisement of a Doctor, on his arrival in the Brazils":

Estimable Brazilians! generous inhabitants of Rio Grande! the celebrated Doctor——, who, in different years, has visited Rio Grande, Porto Alègre and San Francisco has returned to your beautiful province with the firm determination to live and die among you! Generous inhabitants of Rio Grande! do not forget it is the same Doctor who amputated so many arms at Cassapara, so many legs at St. Gabriel, who excised so many jaws at Allegrete, extirpated so many testicles at Rio Pardo, so many breasts at Bargé! And, what is more, if you ask how many deaths followed these colossal operations, ask those who best can tell, and they will answer, Not one! Remember, also, it is the same Doctor who has enlarged the calibre of so many hundred contracted urethras without one relapse! Here, then, here I am! hasten to come to me! In less than seven days, I will make those that urinate in a stream as small as a hair, pass their water the size of a cable; I will treat homœopathically those who desire it; I will cure your fistulas without cutting; I will accept no money when patients die;—in a word I will especially treat all diseases, &c., &c.

Letters to the Editor

UNFORTUNATE NAMES OF HOSPITALS

SIR,—Lately an elderly man was investigated as an inpatient in the throat department of a hospital and found to be suffering from carcinoma of the larynx. It was decided to transfer him direct to the Cancer Hospital for radiotherapy. His wife on arriving home one day found this telegram: "Bed available at the Cancer Hospital." Though she is a stolid woman she was very much upset. The diagnosis of cancer had not been suggested to her before.

Is not there a good opportunity now to change this name and others (such as the Brompton Hospital for Consumption and Diseases of the Chest) which may cause alarm and despondency?

London. A. B.

INFERTILITY DUE TO MECHANICAL FAILURE OF OVULATION

SIR,—The failure of pregnancy to take place in an appreciable percentage of apparently normal women has led to many theoretical discussions on the causes of infertility. In spite of normal ovarian function, revealed by apparently normal basal body-temperature curves, hormone-excretion studies, and normal histological changes in the endometrium, mechanical failure of ovulation may occur regularly in some women and only occasionally in others.

Mechanical failure of ovulation occurs commonly in lower animals. Anyone acquainted with the technique and interpretation of the Friedman test for pregnancy has observed two types of so-called "ovulation" in positive reactions. Usually one sees large round bulging hæmorrhagic follicles lacking apparent rupture points on the surface of the ovary. Endocrinologically, these corpora hæmorrhagica are "normal" in so far as they become functioning corpora lutea. They may, however, contain imprisoned ova, for ovulation, associated with the extrusion of the ovum, has not taken place. In the less common type of positive reaction, especially when an immature rabbit is used for the test, one may find true ovulation points. These appear as tiny almost pinpoint raised bright cherry-red papillæ. They are seldom found on the surface of corpora hæmorrhagica, and develop when mature graafian follicles have ruptured and discharged their ova. The corpora hæmorrhagica that may form under these points after mechanical rupture of the ripe follicles are not so large or so readily seen as the corpora hæmorrhagica which develop in unruptured follicles.

Possibly similar corpora hæmorrhagica and corpora lutea, not preceded by rupture of the follicle, may be found in women. This would explain the occasional records of ovarian pregnancy. In such a case an ovum is probably fertilised by a sperm that penetrates the ovarian capsule, and pregnancy develops without the ovum ever leaving its follicle.

It may be safely assumed that ovulation characterised by rupture of the mature graafian follicle occurs in menstrual cycles in which conception takes place. The basal body temperatures of women who by this criterion have definitely ovulated have been analysed. It will be remembered that body temperature in the few days preceding ovulation in women is slightly but significantly lower than the temperature in the few days after ovulation has taken place. This difference can be demonstrated in all women who appear to have normal cyclical ovarian function.

The mean preovulatory temperature was 97·75 ± 0·40°F in an unselected sample of 22 women under investigation for infertility and in whom conception took place during cycles for which basal body temperatures were available. The mean postovulatory temperature was 98·51 ± 0·34°F. The mean preovulatory temperature was calculated from all of the temperature records of the 22 women during the five-day period before the ovulatory rise began. The mean postovulatory temperature was calculated from all of the temperatures recorded by the 22 women for a five-day period five days after the ovulatory rise began. The difference between

Digitized by Google

the two mean temperatures (0·76 ± 0·05°F) is highly significant, t being 14·97, and P less than 0·01.

The temperature curve obtained by superimposing the 22 known ovulatory temperature curves may be regarded as characteristic of true ovulation, as proved by the onset of pregnancy. The change between the mean preovulatory and postovulatory temperature levels occurred sharply and within a period of twenty-four hours in the 22 women.

The basal body-temperature curves of a patient under observation for infertility show significant differences in the rate of the ovulatory rise of the temperature at the mid-intermenstruum. The mean preovulatory temperature in 12 consecutive menstrual cycles was 98·29 ± 0·29°F, and the mean postovulatory temperature 98·91 ± 0·22°F. The difference (0·62 ± 0·05°F) is highly significant and of the same order as observed for fertile women, t being 12·60, and P less than 0·01. However, the mean daily temperature rose gradually rather than abruptly during the five-day interval between the mean preovulatory and postovulatory temperature phases. A significant rise above the mean preovulatory temperature level did not take place until the fifth day after the start of the change, compared with one day in normal fertile women.

The patient has no demonstrable pelvic pathology. Her tubes are patent, and her basal body-temperature curves and the histological appearance of her endometrium are compatible with regular ovulation and corpus-luteum formation. She has been under the care of many doctors for the investigation and treatment of infertility during the past eight years. Numerous inseminations with seminal fluid containing normal spermatozoa in quantities between 100 and 250 million per ml. have been carried out, without success. It is inconceivable that normal active sperm could have failed to fertilise an ovum at one time or another if ever an ovum had been available. While the cause of her infertility is unknown, it is therefore presumed to be due to mechanical failure of ovulation. It is also believed that the slowly rising type of temperature curve which this patient exhibits may be regarded as an abnormal type of curve associated with the mechanical failure of ovulation.

A more detailed report which is being prepared will include additional experimental evidence in support of this conclusion.

San Francisco, California. ALLAN PALMER.

INDEPENDENCE IN RESEARCH

SIR,—Sir Henry Tizard's inaugural address as president of the British Association, and the *Times* leading article of Sept. 9, both fail to emphasise one most vital factor in the progress of scientific research: it is the virtual suppression in this country of the independent thinker and the laboratories wherein he used to carry out his experiments, and the restriction of facilities for research to such workers as find favour with a small but powerful group of "experts." This narrows the lines of approach and thwarts the efforts of the independent thinker who in the past has supplied nearly all fundamental progress.

I entirely agree with the *Times* on the importance of the biological sciences in the problems of disease in man, animals, and plants. But why then has an independent centre like the Brown Institution—where this fact was recognised and acted on—been suppressed? Probably half the infectious diseases in the world are due to one or another filter-passing virus, and the most fundamental problem in relation to their control is to be able to grow them—apart from other forms of life—according to their physiological requirements.

The writer had an extensive research on this problem mapped out and in progress when in 1944—with the solution clearly indicated in many experiments—the laboratories were destroyed by a bomb. Much of the special apparatus which had been built up was salvaged and now lies idle at Camberley. Why—I ask—have these laboratories not been rebuilt, or some existing building acquired wherein the necessary equipment could be reassembled and the writer given facilities for completing this vast research, possessing, as it does, an economic value of many millions of pounds sterling? It was at the Brown Institution that the writer solved the problem of producing a diagnostic vaccine for Johne's disease of cattle, thereby bringing it under control, and later laid the foundation of much modern work on viruses by the discovery of the "bacteriophage." The research on the growth of the virus group as independent forms of life was being equally successful when the writer was deprived of his post and all facilities for continuing this and other researches on hand.

Camberley, Surrey. FREDERICK W. TWORT.

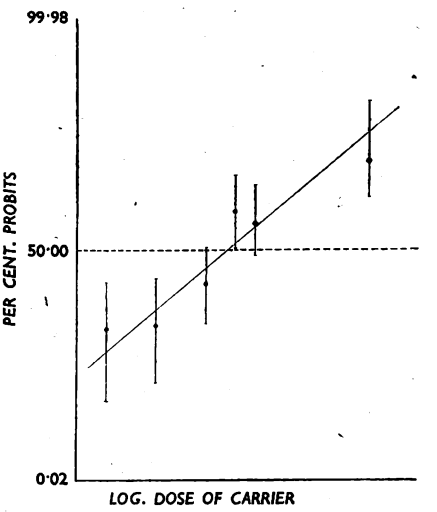
M.R.C.P. EXAMINATION

SIR,—Sir Henry Tidy's thought-provoking and illuminating letter of Sept. 25 interests me very much. I have been amazed to find how rapidly two Censors can uncover my points of weakness in the clinical examination lasting eighty minutes: now I am more amazed that a Censor can in fifteen minutes mark a paper which I, who have just written it, cannot read through in that short space of time. This examination sets out to be a test in clinical medicine; the papers are remarkably clinical in their application, and the clinical itself is certainly a test of powers of observation and ability to make up one's mind, and a battering from two very well-informed gentlemen who want to know how well one's mind is made up and will shatter one's opinion if they can.

A man working in hospital outside the select teaching group has no other opportunity to prove and improve his standard. Experience alone teaches. The clinical examination can be an exhilarating event, even for the candidate who fails; for excellent cases are presented in an atmosphere of such tension that detail is long carried in the mind, and I learn as much in the eighty minutes as otherwise I might in perhaps a fortnight. It is therefore well worth while "having a go" though pounds are scarce and the cost of such a visit to London is high. THRICE TRIED.

ASSESSMENT OF DIPHTHERIA PROPHYLAXIS

SIR,—I have read with interest Dr. Bousfield's article of March 8, 1947 (p. 286) on his clinical trials of Holt's diphtheria prophylactic P.T.A.P. The efficiency of immunising procedures in general, and of diphtheria prophylaxis in particular, can be better evaluated if one utilises certain statistical devices in considering the quantitative relationship between the vaccine potency and the results obtained. In estimating progress in prophylaxis one must take into account the individual differences in reaction; those who are least responsive to immunisation require a relatively very great increase in vaccine potency if inoculation is to be successful.



With regard to diphtheria prophylaxis, an examination of the data given by Hartley[1] for guineapigs shows that when the quantity of toxoid injected was increased from 2·5 Lf to 5 Lf, the Schick-conversion rate rose from 40% to about 85%, but a further increase to 20 Lf only raised the conversion-rate to 93%.

The information supplied by Bousfield revealed a similar phenomenon. He immunised groups of children with 5 Lf of purified diphtheria toxoid adsorbed on to increasing amounts of aluminium phosphate carrier. In this work the increase in Schick-conversion rate

1. Hartley, P. *Wiss. Woche Frankft a. M.* 1934, 3, 81.

Digitized by Google

occurred with increase of *carrier*. When the amount of carrier injected was increased from 0·3 to 0·9 mg. the Schick-conversion rate rose from 12 to 72%; and when the amount was again increased to 7·5 mg. the conversion-rate was 91%.

This phenomenon can be accounted for if allowance is made for the normal distribution of the predisposition to immunity. This distribution accords with the law of normal distribution, or the law of Gauss-Laplace.[2] Applying these equations to Bousfield's figures, we see that the relationship between log. dose (mg. of $AlPO_4$ carrier) and percentage Schick-conversion rate expressed in probits is linear—in agreement with the Gauss-Laplace law (see figure). This statistical finding clearly confirms the consistent progress accomplished by Holt in devising his new diphtheria prophylactic.

Instituto Sieroterapico Italiano, Naples. E. CARLINFANTI.

HOSPITAL ADMISSIONS AND RECORDS

SIR,—The report from King Edward's Hospital Fund, reviewed on p. 578 of your last issue, will be welcomed by records officers, because it recommends the adoption of principles for which those actually engaged in hospital record keeping have been striving for a long while. It implicitly recognises that the job of records officer is a reality. It was, indeed, to achieve just such improvement as this report urges, that records officers up and down the country have formed an Association of Medical Records Officers. They have begun to put their own house in order by pooling their experience and by making arrangements for the more highly trained to provide educational courses for those who are not in touch with modern techniques and for new entrants to the service.

The recommendation that the hospital should have a records committee—elected by the medical committee from among its members and including the chief administrative officer of the hospital and a representative of the nursing staff—should greatly facilitate the work of the lay records officer by encouraging coöperation and providing a channel through which each member of the hospital team can acquaint other members with special difficulties.

The report remarks that there is at present no recognised training for records officers and urges that some regularised course should be agreed upon. An interim course has, in fact, been worked out by our association and a beginning has been made with weekend lecture courses at teaching hospitals at Bristol, London, Manchester, Cardiff, and Sheffield, with further courses to come at Leeds, Newcastle, and other centres. At these courses, to which hospitals within the appropriate regions are invited to send records staff, lectures and demonstrations are given on the following: hospital organisation; office management and selection of staff; appointments system; registration, admission, and discharge procedure; case-history routine; follow-up systems; forms, filing methods, indices, office equipment, and paper control; diagnostic nomenclature; and hospital statistics. It is hoped later to organise full-time training.

B. BENJAMIN
Chairman, Association of Medical Records Officers.

A SIMPLIFIED ROTHERA'S TEST

SIR,—The anticipation and prevention of severe ketosis is so important in the control of diabetes that a simple method of testing for ketone bodies is almost a necessity. The ferric-chloride test has been found unsuitable for use by patients, because (1) to do the test correctly may involve filtering off a precipitate and adding more ferric chloride, a procedure too complicated for many; (2) the colour of a positive reaction is often not properly recognised; (3) the test has many fallacies; and (4) in diabetics where the onset of ketosis is very rapid the test is somewhat too insensitive. Rothera's test is much more satisfactory, provided the patient is warned of its great sensitivity, but the procedure is beyond the mental capacity of some—particularly those who through carelessness or lack of intelligence are liable to slip into a dangerous ketotic state.

To overcome these disadvantages a "powder" test for ketone bodies has been evolved. The most satisfactory composition of the powder has been found to be sodium nitroprusside 0·5%, anhydrous tribasic sodium phosphate 12·5%, and ammonium sulphate 87%. The exact proportions are not important, but the above-mentioned mixture gives a powder which does not develop any interfering colours. It is important, however, to ensure that the salts are dry before they are mixed. Some of this powder has now been kept in a corked bottle for eight months and is still perfectly satisfactory. Some batches deteriorated where adequate care was not taken to ensure that the sodium phosphate was really dry.

The test is carried out by moistening a small pile of the powder with a drop of urine, the colour being read at the end of 3–5 min., a procedure well within the capabilities of the poorest intelligence.

It may be objected that the test is too sensitive—0·02% of acetone just produces a purple colour after 5 min., and the same concentration of diacetic acid produces a definite purple colour. We feel, however, that this sensitivity is an advantage if the patients are told that the final colour must be very dark before they need report. To obviate any mistake, paper of the right colour for comparison is being prepared. The development of the ketosis can be watched by the patient over several days, and so adequate warning of the condition is obtained. Those who are sufficiently intelligent can make appropriate alterations in dosage of insulin and in their diet.

For the past eight months all diabetic patients of one of us (G. A. S.) have been instructed in the use of this powder. Without exception they have all found the test easy to perform, and none are confused by it. It is very rare that even a weak positive result is obtained, but three patients have reported to hospital because of a strong positive result (confirmed in hospital), so enabling the ketosis to be corrected without difficulty.

Armed with this simple test, the diabetic patient should be ensured against going unwittingly into a dangerous diabetic coma.

G. A. SMART
Lecturer in Medicine, Bristol University.
G. H. DARLING
Chief Pharmacist, United Bristol Hospitals.

DIETARY FAT

SIR,—The question of minimum fat requirements in the diet, raised in your issue of Sept. 18, is of great interest. But it cannot be solved simply by experiments which go to show whether there is a lack so gross that it is demonstrable by chemical analysis. Nor is statistical evidence of increased disease incidence of much value. By the time such evidence is available we all know too well that a deficiency exists.

Neither can lack of one factor be divorced from consideration of others. For instance, though our carbohydrates are probably adequate, our protein intake is low.

In this country we have been strictly rationed for eight years now. Before this, limitation of food was unknown; which means that, apart from physical deficiency, the psychological factor must be taken into consideration. Though this latter is occasionally mentioned it is rarely given the prominence it deserves.

Some animals are herbivorous by nature; but most of us prefer to eat meat. In the same way the majority not only like food which requires fat for cooking, but they miss the staying power of the fatty food factor, the last to be digested. Indeed, it is admitted that people feel hungry sooner than they used to do. A race that does not consume much fat presumably cannot have developed that particular desire. Also, it is known that dwellers in hot countries do not require fats in such quantities as those who live in temperate or cold areas.

So far as Europe is concerned experience of ten countries since the war [1] makes me certain that Britain is the worst off, apart from parts of Germany. The Swiss have complained to me that I have misrepresented their fat and meat intake. But this is not the case.

2. See Carlinfanti, E. *J. Immunol.* 1948, **59**, 1, and *Ibid* (in the press).

1. Leyton, N. A Survey of our Subnutrition. *Med. Pr.* 1947, **218**, 331.

Digitized by Google

They were rationed, it is true; but anyone could obtain a meal away from home which would make a couple of English restaurant repasts look very foolish. The same applies in most other places in Europe.

It is clear we shall not die from lack of fat. But, combined as it is with a low protein intake, and a low total calorie diet, there is little doubt that general efficiency is being impaired at a time when it is urgently required.

London, W.1. NEVIL LEYTON.

*** We do not share our correspondent's belief that in Switzerland everybody can afford to eat regularly in restaurants.—ED. L.

UNDER TENSION

SIR,—A Daniel has come to judgment! THE LANCET is going to resolve the international tension. And how. It seems THE LANCET has discovered that England stands between two Great Powers and could act as mediator. One seems to have heard this wishful thought before and not only expressed in English, but in French, Norwegian, Swedish, and, until lately, in Czech. The *late* Dr. Benes and the *late* Mr. Masaryk were most eloquent on this subject. As a preliminary exercise in the rôle of mediator, it might be a good idea if one or two members of the editorial staff tried their hand at reconciling the conflict between Western bourgeois biology and Marx-Leninist biology. They should visit Leningrad, of course. For full measure, THE LANCET offers the reflection that it takes all sorts to make a world. This is the kind of half-truth so common in proverbs. Toleration and an accommodating attitude are admirable qualities in the daily traffic of civilised life, but no one in their senses adopts this easy attitude towards another, who repeatedly attempts to destroy him and who proclaims, fortissimo, his intention of going on trying until he does destroy him. As THE LANCET is fond of proverbs I commend the wisdom of the one about the cobbler and his last.

Bridlington. P. D. H. CHAPMAN.

INDEX FOR FILM RECORDS

SIR,—May I draw your attention to the paragraph under this heading in your issue of Oct. 2?

The use of 35 mm. film and camera for copying documents, journals, &c., should be referred to as "microfilming" and not "photomicrography." The latter term is reserved for the photography of specimens through a microscope system.

The filing system mentioned in your note is of little use for the storage of filmstrips. It is, however, an excellent file for 35 mm. negatives in short lengths (six negatives), and in this sense could be used for storing negatives of filmstrip. A filmstrip proper usually contains more than 20 frames in a continuous length of film.

The proper storage of filmstrips, as opposed to negatives, has offered difficulties in the past, and unfortunately the filing system mentioned does not provide the answer.

Westminster Hospital Medical School, London, S.W.1. PETER HANSELL Director of Medical Photography.

*** We are grateful to Dr. Hansell for pointing our wrong use of the word "photomicrography." As regards his other criticisms of our review, many teachers use short lengths of the film with 2, 4, or 6 pictures because of their flexibility, which longer filmstrips lack. These short filmstrips are useful in building up collections of material and it is for such collections rather than for the long filmstrip that good indexing is specially useful. Dr. Hansell rightly says that the method described is excellent for storing groups of up to 6 negatives; we think it equally useful for filing groups of up to 6 positives.—ED. L.

"... truth which is unpalatable always calls forth persecution. The biologists suffer most, for biology intimately affects man and its truths are usually offensive to his emotions. The physical sciences ... do not generally raise emotional conflicts. ... But the theory of evolution touches their pride and they are not content to disbelieve it for themselves, but eager to suppress its acceptance by others."—*The Medical Officer*, Oct. 2, 1948, p. 143.

Obituary

GEORGE TRENCH WESTERN

M.A., M.D. CAMB.

Dr. G. T. Western died on Oct. 5 at Chalford, Gloucestershire, to which he retired in 1938 from his appointment as physician in charge of the inoculation department of the London Hospital.

He was born in 1877, the son of the late G. A. Western of Shortlands, and he was educated at Monkton Combe and Pembroke College, Cambridge. There he took up rowing, and in 1901 he was spare man for the university boat. It remained one of his enthusiasms, and even when he retired he still took an oar and could exhaust many of his juniors. From Cambridge, where he took the natural sciences tripos in 1899, he went to the London Hospital, and after graduating in 1905 he was appointed one of Prof. William Bulloch's assistants—a distinguished group including Ledingham, Twort, McIntosh, Fildes, and Benians. Bulloch was at that time much interested in Almroth Wright's work on opsonins, and encouraged Western to develop it, giving him the charge of the inoculation department where he was to remain for the next 33 years. His published work included several papers on the treatment of puerperal septicæmia, and he made a considerable study of current methods of raising immunity to tuberculosis. During the first world war he collaborated with L. Rajchman in a special report to the Medical Research Committee (as it was then called) based on 878 cases of bacillary dysentery received from the Eastern Mediterranean.

Working as he did in Professor Bulloch's department in the medical college, Western did none of the routine bacteriological work of the London Hospital, but he was often called in when some special investigation was necessary. His heavy build in no way suggested the deftness he displayed in his bacteriological manipulations, and it came as a surprise to see him extract blood from the smallest vein with a skill that could not be surpassed.

Although a familiar figure to many generations of hospital men, he was less well known as a person—partly, no doubt, because of the isolation of his laboratory in the medical college, but also partly because of an austere and rather discouraging manner in the early days of acquaintance. Climbing was his great passion, and he went to Switzerland every year, except during the war, between 1899 and 1938. In these years he introduced several London Hospital men to climbing, and nothing gave him more pleasure than to see his pupils, after their apprenticeship, become members of the Alpine Club. One of them recalls him as "an exacting instructor, who would never allow carelessness of any sort. His slow and steady walk up to a hut gave an impression of reliability and endurance, but no indication of the ease and grace with which he climbed rocks, moving with effortless speed and rhythm. On off days he was a restful and delightful companion, and on these occasions there was no end to his vivid descriptions of climbs he had done in the past. In 1938, his last climbing year, he was still full of enterprise, and with two others, both of whom he had taught, he did several climbs he had not done before. Only few of those who knew him had the privilege of seeing him in this setting where his outstanding qualities of strength, reliability, and good companionship were so clearly shown."

When war broke out again in 1939 Western left his attractive home in the Cotswolds, and joined the Royal Army Medical Corps as one of its oldest lieutenants. As bacteriologist at the military Hospital for Head Injuries, at Oxford, he retained his London Hospital title of "Daddy Western," but acquired a new ancillary

Digitized by Google

reputation as a most efficient and economical, if autocratic, messing officer, who kept bees and grew vegetables in the hospital garden—and treated everyone alike regardless of rank. As an old member and treasurer of the Cambridge Graduates Medical Club he was to have attended its meeting last week.

He married in 1907 A. S. Carter, and had a son and two daughters.

Diary of the Week

OCT. 17 TO 23

Monday, 18th

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
3 P.M. Dr. F. M. R. Walshe, F.R.S.: Structure of Medicine and its Place among the Sciences. (Harveian oration.)

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
5 P.M. Prof. D. W. Smithers: High-voltage X Rays in the Treatment of Malignant Tumours at a Depth.

SOCIETY OF APOTHECARIES, Black Friars Lane, E.C.4
5 P.M. Prof. D. F. Cappell: Clinical Importance of the Rh Factor.

HUNTERIAN SOCIETY
8.30 P.M. (Talbot Restaurant, London Wall, E.C.2.) Dr. G. R. Mather Cordiner: Rôle of Radiology to the Peptic Ulcer Problem. (Presidential address.)

Tuesday, 19th

SOCIETY OF APOTHECARIES
5 P.M. Mr. H. Osmond-Clarke: Rehabilitation of the Physically Injured.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. F. Ray Bettley: Papular Dermatoses.

SOCIETY FOR THE STUDY OF ADDICTION
4 P.M. (11, Chandos Street, W.1.) Dr. J. Yerbury Dent: Treatment of Anxiety and Addiction by Apomorphine.

Wednesday, 20th

ROYAL COLLEGE OF SURGEONS
5 P.M., Prof. J. Paterson Ross: Surgery of the Sympathetic Nervous System.

SOCIETY OF APOTHECARIES
5 P.M. Dr. Macdonald Critchley: Modern Treatment of Some Neurological Disorders.

HARVEIAN SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Dr. Samuel Oram: Pulmonary Embolism.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. Peter Henderson: Epilepsy in Children.

UNIVERSITY OF GLASGOW
8 P.M. (Department of Ophthalmology.) Dr. Byron Smith: Plastic Surgery of the Eyelids.

Thursday, 21st

ROYAL COLLEGE OF SURGEONS
5 P.M. Mr. P. H. Mitchiner: Surgery of Sepsis.

SOCIETY OF APOTHECARIES
5 P.M. Dr. R. R. Trail: Treatment of Pulmonary Tuberculosis.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26, Portland Place, W.1
7.30 P.M. Dr. J. T. Duncan: Epidemiology of Fungus Diseases. Dr. Isaac Muende: Treatment of Fungus Diseases.

BRITISH ORTHOPÆDIC ASSOCIATION
10.30 P.M. (Queen's University, Belfast.) Prof. George Perkins: Painful Shoulder.
2 P.M. (Whitla Medical Institute, Belfast.) Short papers.

HONEYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Mr. Joe Pennybacker: Intracranial Tumours in the Aged.

Friday, 22nd

WEST LONDON MEDICO-CHIRURGICAL SOCIETY
8.30 P.M. (South Kensington Hotel, 41, Queen's Gate Terrace, S.W.7.) Dr. W. S. C. Copeman: West London Worthies—a Retrospect. (Presidential address.)

MIDDLESEX COUNTY MEDICAL SOCIETY
3 P.M. (Hillingdon Hospital, Uxbridge.) Miss J. Morgan: Report on 450 Cæsarean Sections. Mr. K. S. Mullard: Carcinoma arising in Segmental Bronchi.

BRITISH ORTHOPÆDIC ASSOCIATION
9.20 A.M. (Whitla Medical Institute, Belfast.) Short papers.
11 A.M. Mr. S. A. S. Malkin: Presidential address.
2 P.M. (Royal Victoria Hospital.) Clinical demonstrations.

Saturday, 23rd

NUTRITION SOCIETY
10.30 A.M. (Royal Society of Arts, John Adam Street, W.C.2.) Discussion on Anti-vitamins in Food.

BIOCHEMICAL SOCIETY
11 A.M. (London School of Hygiene, Keppel Street, W.C.1.) Symposium on Partition Chromatography and its Application to Biochemical Problems.

BRITISH ORTHOPÆDIC ASSOCIATION
9.20 A.M. (Whitla Medical Institute, Belfast.) Short papers.

Notes and News

MEDICAL RECRUITS

THE Central Medical War Committee has been informed that, on the recommendation of the Medical Priority Committee, the Minister of Health, with the concurrence of the Secretary of State for Scotland, has decided that the emergency arrangements under which a young practitioner liable for military service is recruited after six months' tenure of an "A" post will cease at the end of October. Young practitioners completing their tenure of "A" posts on or after Nov. 1, and selected for appointment to "B2" posts, will be granted deferment of call-up in accordance with the regulations in operation before the introduction of the emergency arrangements last July.[1] Hospital authorities are being informed by circular letter of this change in procedure. There is, however, no change in the arrangement under which young practitioners approaching the age of 26 on qualification are recruited before their 26th birthday, even if this should prevent their completing an "A" post or occupying an "A" post at all.

THE TEAM SPIRIT IN HOSPITAL

IN an address opening the new session of the Royal Free Hospital, London, on Oct. 1, Mr. L. E. C. Norbury, senior surgeon to the hospital and a vice-president of the Royal College of Surgeons, spoke on the importance of team-work. In a hospital, he said, the work of each department is a means to a common end, and each department is an essential unit in the team. On entering the medical school the student is initiated into the team, and the team spirit should be inculcated from the earliest days—though the process of initiation may be unexpected and something of an ordeal.

In Mr. Norbury's opinion more use should be made of the services of professors and teachers of the preclinical subjects, as members of the team, in discussions and demonstrations. He recalled a series of lecture-demonstrations, held some years ago at the Royal Free, in which clinical and preclinical teachers dealt with the subject from their particular angles. "To my mind such a discussion by various members of a team, and the pooling of knowledge, is of far greater practical value to all concerned than a stereotyped lecture. The pendulum is already swinging in this direction, and I look forward to the day when the old formal series of lectures will be replaced entirely by lecture-demonstrations along the lines indicated. It is the practical application of knowledge which should be instilled into the mind of the student. The textbook can be studied at home and at leisure."

In a properly conducted team there must be common service and common loyalty, and in arriving at a satisfactory plan of campaign there must be discussions and consultations with free expression of opinions. Such cultivation of the team spirit was essential for progress in medical science. In a recent speech Mr. Herbert Morrison had said: "If we could bring into every factory and mine and farm and workshop the spirit and enthusiasm that the ordinary man brought to team games half our troubles would be over," and these sentiments, Mr. Norbury believed, could usefully be applied to medicine. In a well-appointed team there must, moreover, be time for relaxation and social enjoyment: its members must "work in harmony both socially and intellectually in order to produce the optimum results."

PHARMACOLOGICAL RELATIONSHIPS

THE Society of Chemical Industry has formed a fine-chemicals group, and at the first meeting, held in London on Oct. 5 with Sir Jack Drummond, F.R.S., in the chair, an inaugural address was delivered by Dr. J. H. Burn, F.R.S., professor of pharmacology in the University of Oxford. He said he had always believed that the university worker should be willing to assist industrial laboratories if he could, as a matter of public service. One of the contributions made by university pharmacological laboratories to advance in the fine chemical industry was the introduction of methods of biological standardisation, and tribute was due to Sir Henry Dale in gaining acceptance for the principle of comparative methods and of the necessity for international standards.

Another contribution, he said, stemmed from the classical work of Dale and Laidlaw, and their chemical colleagues Carr, Barger and Ewins, on adrenaline and sympathomimetic

1. See *Lancet*, 1948, i, 930, 971.

Digitized by Google

amines, and on histamine and acetylcholine. More and more did it appear from subsequent work that adrenaline, histamine, and acetylcholine were three substances which the body used for many different purposes. It now appeared that the action of a large number of chemical substances in the body was to modify or interfere with the action of adrenaline or histamine or acetylcholine. It seemed possible that local anæsthetics and analgesics were substances which antagonised the action of acetylcholine at sensory nerve-endings, or in other parts of the central nervous system and that the power of substances to lengthen the refractory period of heart muscle might be related to their antagonism to acetylcholine in the metabolism of cardiac tissue.

The interrelation of properties of local anæsthetics, spasmolytics, and analgesics made it worth examining all compounds prepared to exert one of these properties for its possession of the others. A substance introduced as a local anæsthetic might be, for example, a still better spasmolytic. It was probably because anti-histamine substances possessed the other properties that they produced side-effects. If they were also analgesics it was not surprising that they caused mental confusion and depression, and if they were atropine-like it was not surprising that they caused dryness of the mouth.

One other way in which the grouping together of many properties as fundamentally the same was useful was that it brought some order into the long list of apparently unrelated plant alkaloids. The similarity in many properties of atropine, papaverine, and quinine, and of conessine from kurchi bark and quinine, suggested points of biochemical similarity, thus assisting towards an understanding of relationships. These examples surely justified the pharmacologist studying the actions of acetylcholine, histamine, and adrenaline in the body. Similar studies were likely also to advance the practically important subject of chemotherapy.

University of London

Mr. E. M. Crook, PH.D., gave the first of four public lectures at University College, Gower Street, W.C.1, on the Electron Microscope and its Biological Applications. The other lectures will be given on Mondays, Oct. 18, 25, and Nov. 8, at 4.45 P.M. On Friday, Nov. 5, at 5 P.M., Prof. G. Levi, of the University of Turin, will deliver a lecture on Relations of Interdependency between various parts of the Nervous System in the Embryo and in the Adult.

Dr. Robert Cruickshank has been appointed to the chair of bacteriology at St. Mary's Hospital medical school as from Jan. 1.

Dr. Cruickshank, who is 49 years of age, was educated at Strichen secondary school and the University of Aberdeen where he graduated M.B. with honours in 1922. For the next two years with an Alexander Anderson fellowship he worked at Aberdeen and at Glasgow where he later became resident medical officer at the Royal Hospital for Children and assistant medical officer at Belvidere Infectious Diseases Hospital. In 1925 he graduated as M.D. with highest honours. He held the McRobert lectureship in cancer research at Aberdeen in 1927, and in the same year he was the first recipient of the Hutchison prize for his essay on intestinal flora of children. In 1928 he was appointed lecturer in bacteriology in the University of Glasgow, and he also held the post of bacteriologist to the Glasgow Royal Infirmary. In 1936 he came to London as pathologist to the group laboratory at the L.C.C. North-Western Hospital. Three years ago he was appointed the first director of the central laboratory of the Public Health Laboratory Service at Colindale, and during the past three years he has also been acting as an extramural teacher at the London School of Hygiene. In 1933 Dr. Cruickshank delivered at the Royal College of Physicians the Milroy lectures on Pneumococcal Infections. He was a Chadwick lecturer in 1943 and gave the Frederic Still lecture on Infection in Infancy to the British Pædiatric Association in 1945. His other published work includes papers on the biology of the vagina, bacterial infection of burns, staphylocoagulase, diagnosis of pertussis, the aerial spread of infection, and the control of dust-borne streptococcal infections. He was joint editor of THE LANCET manual on *Control of Common Fevers* and a sectional editor of *Recent Advances in Clinical Pathology*. In 1946 he was elected F.R.C.P.

University of Leeds

The annual dinner for past and present students of the medical school will be held at the Great Northern Hotel, Leeds, on Friday, Nov. 26, at 7.30 P.M. Dr. J. T. Ingram will preside and Lord Moran will be the principal speaker. Tickets may be obtained from the secretary of the Students' Representative Council at the school before Nov. 14, 1948.

Medical Practitioners' Union

Dr. Bruce Cardew has been appointed general secretary to the Medical Practitioners' Union and editor of the *Medical World* in place of Dr. A. Welply, who has retired.

Royal College of Physicians of London

A course of lectures will be given at the college, Pall Mall East, S.W.1, at 5 P.M. daily from Nov. 2 to Dec. 17. Applications should reach the registrar by Oct. 25.

Westminster Hospital and Medical School

The annual dinner for past and present students was held in London on Oct. 2 with Sir Arnold Stott in the chair. The speakers included Mr. G. H. Macnab (dean of the Medical school), Mr. H. E. Harding (subdean), and Sir Adolphe Abrahams.

Northern Ireland Health Service

In Northern Ireland about $1^1/_4$ million people—93% of the population—have placed their names on doctors' lists under the health scheme. These figures have been given by Mr. William Grant, minister of health and local government, who said that 730 doctors had so far joined the service.

National Marriage Guidance Council

Miss Phyllis Bottome will deliver the Donald Gillies lecture at the Royal Society, Burlington House, London, W.1, on Wednesday, Oct. 20, at 6 P.M. She is to speak on Love and Marriage. Sir Eardley Holland will be in the chair.

Scottish Society of the History of Medicine

A meeting of this society will be held at the Royal Faculty of Physicians and Surgeons, 242, St. Vincent Street, Glasgow, on Wednesday, Oct. 20, at 5.30 P.M., when Prof. J. D. Mackie will speak on the History of Glasgow, and Mr. A. L. Goodall on the History of the Faculty.

St. George's Hospital

Dr. Anthony Feiling and Dr. Desmond Curran are to give a series of lecture-demonstrations in neurology and psychiatry at the medical school during the autumn term on Thursdays at 4.30 P.M. They are open to all doctors and senior students.

Parentcraft in the Home

The National Association of Maternity and Child Welfare Centres and for the Prevention of Infant Mortality is holding a conference on this subject at the Y.W.C.A., Great Russell Street, London, W.C.1, on Friday, Oct. 22, at 10.30 A.M. Dr. Leslie Housden will be in the chair.

Royal Society of Medicine

Norman Gamble Fund.—The committee of award will shortly consider applications for grants from this fund in aid of research in otology. Applications should reach the secretary of the society, 1, Wimpole-street, London, W.1, from whom further particulars may be had, not later than Nov. 25.

King Edward VII's Hospital for Officers

Queen Mary is reopening this hospital at Beaumont House, Beaumont Street, London, W.1, today, Oct. 15. The hospital has 2 wards of five beds and 2 of two beds, where nursing and maintenance will be free. There are also 17 single rooms where a charge will be made. Patients make their own arrangements with their physicians and surgeons. Regular and retired officers of the three Services are eligible for admission; also all temporary officers who fought in the 1914–18 or 1939–45 wars provided they become subscribers. Applications should be made to the house-governor.

Alamein Village Settlement

In his address to students at the annual prize-giving of Charing Cross Hospital on Oct. 7, Field-Marshal Viscount Montgomery of Alamein referred to the Alamein Village Settlement intended largely for men discharged from the Services because of tuberculosis. It will be run, he said, in conjunction with the existing village settlement at Enham, near Andover, Hants, which was established for disabled men after the first world war. It is hoped that accommodation will be found for 500 ex-Service personnel who will be taught a trade and given the opportunity of partaking in the industries of Enham. There will be a hostel for the men without families, cottages for those with families, a village club, a church, and a hospital.

Digitized by Google

Planning Forum

The autumn series of lectures to be held in the Planning Centre Hall, 28, King Street, Covent Garden, London, W.C.2, includes discussions on the Kinsey Report by Mr. David Mace, PH.D., Dr. Fred Grundy, and the Rev. J. Leycester King (Oct. 27); on Population and Emigration by Dr. David Glass, Prof. Brinley Thomas, and Mr. R. J. Goodman (Nov. 11); and on Work and Health by Dr. R. S. F. Schilling, Mr. Brian Bunch, A.R.I.B.A., and Dr. John Burton, with Prof. J. M. Mackintosh in the chair (Nov. 24). The lectures are held on the fourth Wednesday and second Thursday in each month at 6.15 P.M., and further particulars may be had from the centre.

S.M.A. on Health Centres

The council of the Socialist Medical Association has passed a resolution which welcomes the recognition by the council of the British Medical Association of the need for health centres, and continues:

> The Socialist Medical Association supports the urgent demand put forward for an experimental trial of different types of health centre in varying areas, but is strongly opposed to the view that widespread development of health centres should not be commenced until after such experiments are completed. The further development of general practice depends on health centres, and these, in accordance with the Act, must be set up and properly equipped by the local health authorities, and not left to individual groups of practitioners whose association would not be under democratic control.

Minister on Health Service

On Oct. 7, addressing the first annual meeting of the Executive Councils' Association (England) of the National Health Service, Mr. Aneurin Bevan, Minister of Health, again appealed to the public to use the service prudently, intelligently, and morally; he described it as a test of the maturity of the British people. As reported in the *Times*, he went on to speak as follows of the general practitioner's responsibility. "Over-prescribing can be as bad as under-prescribing. Some general practitioners are very conscious of the impressiveness of long lists of drugs in their prescriptions on the psychology of their patients. We want the general practitioner to prescribe what he believes is necessary, and put nothing in his way—but we want to impress upon him that it is not a good thing to evoke merely a psychological response by prescribing too expensive drugs." In the N.H.S., he said, the number of prescriptions is approaching twice what it was under National Health Insurance. At the present rate over 140–150 million prescriptions would be dispensed annually.

On Oct. 6 the Minister of Health met the chairman of boards of governors of teaching hospitals, regional hospital boards, and hospital management committees. This was in response to a personal invitation from the Minister, who is anxious to make regular contact with as many as possible of those who now share responsibility for running the National Health Service. Mr. Bevan stressed that their responsibility lay, first and foremost, with the patient, and this must never be forgotten or overlooked.

Cambridge Graduates Medical Club

This club held its annual meeting at Downing College on Oct. 6. Presiding over some 65 members at the dinner, Mr. W. H. C. Romanis recalled that from 1930 until the war the club met once a year at Cambridge. Sir Lionel Whitby, master of Downing and regius professor of physic, who was the principal guest, said that the club's function was mainly social: it provided an opportunity to revisit Cambridge and meet old friends. While Oxford had become an industrial city, Cambridge remained an overcrowded market town, without the advantages or the disadvantages of wealth. The medical school, full to overflowing, was incomparably more difficult to enter than in "our day," and the examinations were so much more difficult that he was glad to be on the right side of the table. The main innovation was the institution of a postgraduate school. Having secured recognition of Addenbrooke's as a teaching hospital, the next task had been to develop departments specially appropriate to Cambridge—first in radiotherapeutics (associated with physics) and in experimental medicine (associated with physiology and biochemistry). The new department of human ecology was not only making epidemiological and statistical studies of the peculiar problems of the fenland but had also undertaken the preventive medical care of undergraduates. He hoped in due course to see departments of pædiatrics and of hæmatology. The policy adopted was to take one step at a time, obtaining funds through normal channels. It remained to be seen whether Cambridge would ever have a full undergraduate medical school; but certainly it could not do so till Addenbrooke's was rebuilt—for which there were schemes involving a 100-acre site and 1200–1500 beds. In conclusion Sir Lionel Whitby spoke of the difficulties to be expected if the scale of academic salaries remained at its present level, so low in relation to the rewards to be expected in quite ordinary specialist practice.

Colonial Medical Research Studentships

The Secretary of State for the Colonies has instituted a limited number of these studentships for graduates in medicine and cognate sciences, who wish to prepare themselves for research work in tropical medicine and related subjects. It is the intention that students satisfactorily completing their courses shall be offered posts in the projected Colonial Research Service. Application should be made, through the head of the candidate's department, to the Secretary, Colonial Medical Research Committee, c/o Research Department, Colonial Office, Sanctuary Buildings, Great Smith Street, London, S.W.1.

Dr. D. J. A. Alban-Jones has been awarded scholarships by the Belgian and Netherlands governments through the British Council to study obstetrics and gynæcology. He is to work at the Hôpital St. Pierre in Brussels for eight months, and he will then spend four months in Amsterdam.

Following representations by the Medical Defence Union, Messrs. Silten Ltd., the manufacturers of 'Leucotropin' have expressed regret that a pamphlet advertising this product quoted from a book by Prof. L. S. P. Davidson and Dr. J. J. R. Duthie, without authority and in such a way as to give the impression that these authors advocated the use of leucotropin and had composed the pamphlet.

British Drug Houses ask us to state that free copies of their *Guide to the B.P. 1948* will be sent to doctors who apply to their offices at Graham Street, City Road, London, N.1.

Births, Marriages, and Deaths

BIRTHS

CANE.—On Oct. 4, in London, the wife of Dr. C. S. Cane—a son.
CUMMING.—On Sept. 30, in Edinburgh, the wife of Dr. R. A. Cumming—a son.
FRANKLIN.—On Oct. 4, in London, the wife of Dr. John Franklin—a daughter.
GINSBORG.—On Oct. 4, in London, the wife of Dr. S. Ginsborg—a son.
HART.—On Oct. 5, in London, the wife of Dr. F. D. Hart—a daughter.
LANE.—On Oct. 7, the wife of Dr. Roger Lane—a daughter.
ROBINSON.—On Oct. 2, at Slough, Bucks, the wife of Dr. A. B. Robinson—a son.
ROGERS.—On Oct. 7, in London, the wife of Dr. John Rogers—a daughter.
RUSSELL.—On Oct. 5, at Nottingham, the wife of Dr. Manson Russell—a son.
SWINNEY.—On Aug. 28, in Albuquerque, New Mexico, the wife of Mr. John Swinney, M.C., F.R.C.S.—a son.

MARRIAGES

HEWLETT—BARRACLOUGH.—On Sept. 29, at West Byfleet, Henry Reynardson Hewlett, lieut.-commander, R.N., to Patricia Mary Barraclough, M.B.

DEATHS

DINGLE.—On Oct. 2, Frederick Robert Dingle, M.R.C.S.
HANNAY.—On Oct. 5, in London, Robert Strickland Hannay, C.B., C.M.G., D.S.O., L.R.C.P.E., major-general, late R.A.M.C. retd, aged 77.
HEMSTED.—On Oct. 7, at Kintbury, near Newbury, Berks, Edmund Spencer Hemsted, M.R.C.S., aged 78.
MCCARTHY.—On Oct. 3, at Sidmouth, John McDonald McCarthy, M.B. Camb., colonel, R.A.M.C. retd, aged 75.
MALCOLM.—On Oct. 6, in Edinburgh, John Wright Malcolm, O.B.E., M.C., M.B. Edin., lieut.-colonel, R.A.M.C. retd, aged 56.
PORTER.—On Oct. 4, at Bristol, Charles Porter, M.A. Oxfd, M.R.C.S.
ROBERTS.—On Oct. 7, in London, Alexander Boyd Roberts, M.D. McGill.
STEPHENS.—On Oct. 8, at Newquay, Cornwall, William John Stephens, M.R.C.S., aged 82.
WESTERN.—On Oct. 5, at Chalford Hill, Stroud, George Trench Western, B.A., M.D. Camb.

Digitized by Google

OCT. 23, 1948 PAGES 635 TO 674

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6530 LONDON: SATURDAY, OCTOBER 23, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Meningococcosis: a Protean Disease
H. STANLEY BANKS, F.R.C.P. 635

Infection by Penicillin-resistant Staphylococci
MARY BARBER, M.D.
MARY ROZWADOWSKA-DOWZENKO, M.D. 641

Carotid-sinus Syndrome
RICHARD TURNER, M.R.C.P.
Prof. J. R. LEARMONTH, F.R.C.S.E. 644

Fatal Staphylococcal Enteritis Developing during Streptomycin Therapy by Mouth
I. R. H. KRAMER, L.D.S. 646

Treatment of Local Infection with Diamidines
F. KOHN, M.D.
CLARA D. CROSS, M.R.C.P. 647

Alginates in Endaural Wound Dressing
E. R. G. PASSE, F.R.C.S.
GEORGE BLAINE, L.R.C.P.E. 651

SPECIAL ARTICLES

The Structure of Medicine 660
The Transvaal Hospitals Dispute 661
Poliomyelitis in New Zealand 662
Refresher Courses for General Practitioners 662

REVIEWS OF BOOKS

The Mechanism of Abdominal Pain. V. J. Kinsella, F.R.C.S. 652
Present Status of the Surgical Treatment of Hyperthyroidism. Prof. W. H. Cole, M.D., Edson Fowler, M.D. 652
Jaundice. E. R. Movitt, M.D. 652
Introduction to Diseases of the Chest. James Maxwell, F.R.C.P. 652

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 664

LEADING ARTICLES

PREFRONTAL LEUCOTOMY 653
ADVANCES IN MICROSCOPY 654
RECOVERING FROM TUBERCULOSIS 655

ANNOTATIONS

The Prentice Practitioner 656
Psychogenic Rheumatism? 657
Sheep Street 657
B.C.G. for Nurses 657
Aseptic Dispensing 658
M.O.H. 658
Of Dying 658
Œstrogens in Diabetes 659
War Casualties 659
The Distinction Awards 659

DISABILITIES

15. Deafness 663

PUBLIC HEALTH

Mobile Maternity Centres 664
Poliomyelitis in the U.S.A. 664
The Second Quarter 664

LETTERS TO THE EDITOR

M.R.C.P. Examination (Dr. L. W. Batten) 665
Infantile Gastro-enteritis Treated with Streptomycin by Mouth (Dr. I. M. Anderson and others) 665
Transverse Myelitis Complicating Pneumonia (Mr. A. S. Aldis, F.R.C.S.) 666
Proprietary Medicines under the National Health Service Act (Mr. E. W. Godding) 666
Medical Secretaries 667
Anomaly of Abdominal Musculature (Mr. A. W. Adams, F.R.C.S.) 667
Under Tension (Dr. Ranyard West) 667
How Many Nurses? (Miss M. M. Edwards, S.R.N.) 667
Abortion, Sterilisation, and the Law (Dr. Norman Haire) 668
Tests for Thiouracil Sensitivity (Dr. E. K. Blackburn and others) 668
Compulsory Admission 669
Regional Specialist Committees (Dr. V. C. Cornwall) 669
The Young Consultant 669
Medical Records (Dr. J. V. S. A. Davies) 669
Dentures and Anæsthesia (Dr. H. Parry-Price) 670

OBITUARY

John William Scott Macfie 670
Charles Edward Lacey 670
Sir Bruce Bruce-Porter 670
The late Dr. Western 671

NOTES AND NEWS

Protective Fears 671
Social and Preventive Medicine in England 671
Union of St. Luke 672
Cleaner Food 672
Necropsy on a Transfixionist 672
Ambulance and Fire Services 672
Homes for the Aged in London 672
Malarial Control in Sardinia 672
International Scientific Film Congress 672
School of Pharmacy 672

University of London 672
University of Liverpool 673
University of Sheffield 673
Royal College of Physicians of London 672
Royal College of Surgeons of England 673
Royal College of Obstetricians and Gynæcologists 673
Royal Medico-Psychological Association 673
More Nurses and Midwives 673

Diary of the Week 674
Appointments 674
Births, Marriages, and Deaths 671

PENICILLIN: ITS PROPERTIES, USES AND PREPARATIONS

Deals with Manufacture, Chemistry, Stability, Standards, Pharmacology, Clinical Use, Pharmaceutical Preparations and Legal Aspects

Pp. 199 Illustrated Price 10s. 6d. (postage 6d.)

"Seldom has so much information been compressed into two hundred pages . . ."—THE LANCET

EXTRA PHARMACOPŒIA (MARTINDALE)

In two volumes 22nd edition

Vol. 1. Pp. 1289. For the Clinician.

Vol. 2. Pp. 1217. For the Biochemist and Pathologist.

Price per volume 27s. 6d. (postage: 1 vol. 9d., 2 vols. 11d.)

THE PHARMACEUTICAL PRESS, 17, BLOOMSBURY SQUARE, W.C.1

Publishers of the British Pharmaceutical Codex

Digitized by Google

RADIOACTIVE INDICATORS

Their Application to Biochemistry, Animal Physiology and Pathology

By G. HEVESY

Institute for Research in Organic Chemistry, University of Stockholm, and Institute of Theoretical Physics, University of Copenhagen

CONTENTS (abbreviated): Production of Radioactive Indicators. Radioactive Indicators of possible Interest in Tracer Work. Determination of Radioactivity. Atomic Interchange. Application of Isotopic Indicators in Chemical Analysis. Application of Isotopic Tracers in the Study of Absorption, Distribution, and Secretion. Application of Isotopic Indicators in the Study of Permeability of Phase Boundaries. Turnover Studies. Path of Intermediary Reactions. Skeleton Metabolism. Application of Radioactive Indicators in the Study of the Red Corpuscles. Shortcoming of the Radioactive Tracers. Tables—Index.

1948 400 pages 129 tables 60/-

MATHEMATICS OF THE GENETICS OF POPULATIONS

By G. DAHLBERG

State Institute of Human Genetics, Uppsala, Sweden

CONTENTS: 1. Division of characteristics from a hereditary viewpoint. 2. The conception of race and the laws of Mendel. 3. Different forms of inheritance. 4. Composition of populations in panmixia. 5. The effect of mutations on the composition of a population in panmixia. 6. The effect of selection on a population. 7. Selection and mutations. 8. The effect of inmarriage on a population. 9. Inmarriage and selection. 10. Assortative mating. 11. Assortative mating, inmarriage, selection, and mutations. 12. The importance of the isolate for the composition of populations. 13. Isolates and race. 14. Mutations, selection, and isolates. 15. Isolates and inmarriage. 16. Isolates, assortative mating, and selection. 17. General survey.

Published by S. Karger, Basel, Switzerland

1947 182 pages 31 tables 31/6

Structure et activité pharmacodynamique des

MÉDICAMENTS DU SYSTÈME NERVEUX VÉGÉTATIF

Adrénaline, Acétylcholine, Histamine et leurs Antagonistes

par D. BOVET et F. BOVET-NITTI

Institut Pasteur, Paris—Istituto Superiore di Sanità, Rome

Published by S. Karger, Basel, Switzerland

1948 840 pages 106/-

INTERSCIENCE PUBLISHERS, LTD.

2a SOUTHAMPTON ROW · LONDON, W.C.1

New and Standard BAILLIÈRE Books

Medical Publishers since 1826

BUCHANAN'S

Manual of Anatomy:

Including Embryology

Revised and largely rewritten by F. WOOD JONES, D.Sc., F.R.S., F.R.C.S. 7th Ed. Pp. viii+1,616. 847 Illustrations. 48 Plates. Over 250 new drawings. **45s.**

TREDGOLD'S

Mental Deficiency (Amentia)

7th Ed. Pp. xvi+534. 45 Plates. **30s.**

"As a textbook the work deserves high praise."—*The Lancet.*

NICOLE'S

Psychopathology

A Survey of Modern Approaches. 4th Ed. Pp. xii+268. **15s.**

"We can confidently recommend this book."—*Post Graduate Medical Journal.*

WOOD JONES'

The Hand

(The principles of anatomy as seen in the hand.) 2nd Ed. Pp. xii+418. 2 Plates. 144 Illustrations. **25s.**

ROSE AND CARLESS'

Manual of Surgery

Edited by Sir CECIL WAKELEY, K.B.E., and J. B. HUNTER, C.B.E. 17th Ed. Pp. 1,766. 1,100 Illustrations. 30 Coloured Plates. (Two Vols.) **35s.**

STOCKINGS'

The Metabolic Brain Diseases and their Treatment

Pp. viii+262. **16s.**

"Every practitioner in the medical field must examine Dr. Stockings' opinions."—*Medical World.*

LAKE'S

The Foot

3rd Ed. Pp. viii+432. 136 Illustrations. **15s.** A manual dealing with the evolution, anatomy, physiology and diseases of the foot in theory and practice.

THE UFAW HANDBOOK on the Care and Management of Laboratory Animals

Edited by ALASTAIR WORDEN, M.A., B.Sc., M.R.C.V.S. Pp. xvi+368. 70 Illustrations. **31s. 6d.**

"This is an outstanding book, and one of which British medicine and veterinary science may be proud."—*The Lancet.*

MACKENNA'S

Diseases of the Skin

Revised and enlarged by R. M. B. MacKENNA, M.A., M.D., M.R.C.P. (Lond.). 4th Ed. Pp. xiv+557. 46 Coloured Plates. 168 Illustrations. **25s.**

PARKER'S

Textbook of Clinical Pathology

(Formerly Kracke and Parker.) Edited by the late FRANCIS P. PARKER, M.D., and includes sections contributed by eight eminent American pathologists. 3rd Ed. Pp. xx+1,023. 229 Illustrations, Photographs and Diagrams. 64 Colour Plates. **50s.**

COX'S

Atlas of Practical Incisions and Some Operative Procedures

Pp. viii+85 (11"×8"). 61 Illustrations. **16s. 6d.** By means of beautifully executed drawings and photographs, the author presents incisions and operative procedures.

KELLY'S

Encyclopædia of Medical Sources

The author lists accurately with title and complete reference the outstanding contributions to medical knowledge together with medical eponyms such as culture media, methods, operations, signs, syndromes, tests, &c. Pp. v+476. **41s.**

Baillière, Tindall & Cox, 7-8 Henrietta Street, London, W.C.2

Digitized by Google

MENINGOCOCCOSIS

A PROTEAN DISEASE*

H. STANLEY BANKS
M.D. Glasg., F.R.C.P., D.P.H.
PHYSICIAN-SUPERINTENDENT, PARK HOSPITAL, HITHER GREEN

RECOGNITION of the protean nature of infections is usually slow. The dominant clinical form may long be thought of as the complete disease. In most cases the concept soon becomes widened by inclusion of the more obviously related clinical forms; but it is only after protracted clinical observation and laboratory study that the rarer forms are revealed in their true relation to the disease complex. This ever-widening conception of a disease has long been familiar in tuberculosis and syphilis. We are witnessing it today in glandular fever and poliomyelitis. I think it is no less true of meningococcal disease.

"Cerebrospinal meningitis," "epidemic meningitis," and "cerebrospinal fever" are terms representing successive expansions of the idea of this disease. The Waterhouse-Friderichsen syndrome and scattered cerebral suppuration represent later accretions. Chronic meningococcal septicæmia was firmly added only during the late war. The encephalitic forms, the hæmorrhagic and non-hæmorrhagic adrenal forms, the pituitary and other metastatic lesions are all comparatively recent conceptions. "Cerebrospinal fever" is a designation no longer adequate for the disease as a whole. "Meningococcal disease" is an inclusive term but somewhat colourless. The protean nature of the disease and its broad pathology seem to justify "meningococcosis" as a generic name for all forms of the disease on the analogy of tuberculosis, trichinosis, and the like.

The basis of these lectures is a series of 706 consecutive cases admitted to the Park Hospital between Jan. 1, 1939, and June 30, 1947, a period of stabilised treatment with the more active sulphonamides, and, in the later years, with systemic penicillin in a few selected cases. Serum treatment was not used in any case, having been rejected as unnecessary during the experimental period of chemotherapy in 1937–38.

The series is mainly a civilian one of the usual varied age-distribution from infancy to over 70 years of age, but contains a number of Service cases which slightly overload the young adult groups. This is balanced, however, by the higher than normal incidence of older persons admitted during the war and the evacuation, when many young persons were absent from London. The period includes pre-epidemic, epidemic, and post-epidemic phases. The greatest pressure of the epidemic phase came in the first four months of 1940, when 120 patients were admitted, of whom 12 died, 6 being infants—a case-fatality rate of 10%. This is somewhat higher than the case-fatality rate for the whole period (7·36%).

TABLE I—RESULTS IN 706 CONSECUTIVE CASES OF MENINGOCOCCAL DISEASE ADMITTED TO PARK HOSPITAL 1939–47

Age-group (years)	No of cases	No. of deaths	Fatality-rate (%)
0–1	76	18	23·7
1–2	43	2	4·6
2–3	47	2	4·2
3–4	45	3	6·6
4–5	31	2	6·4
5–15	90	3	3·3
15–25	171	6	3·5
25–35	92	5	5·4
35–45	45	4	8·8
45–55	36	2	5·5
55–65	19	2	10·5
65–75	11	3	27·2
Total	706	52	7·4

It should be noted that no case has been excluded from the series, even though the patient was moribund on admission.

Table I shows the age-incidence and fatality in single years up to 5 years of age, and in ten-year periods thereafter. This illustrates some general principles of the epidemiology of the disease: (1) there are far more cases in infants under a year than in any other single year of age; (2) incidence declines with age, except for the period 15–25 years, which contains more cases than the previous decade; (3) after the age of 35 there is a sharp drop, and after the age of 55 another and still sharper drop in incidence; and (4) case-fatality rates are high only at the extremes of life, the curve of mortality from infancy to old age being cup-shaped, with its lowest level between 15 and 25 years.

Fig. 1 shows the curves of notifications of cerebrospinal fever during 1936–45 and indicates the general epidemiological background of the series. The years 1940–42 were the epidemic years, each with a characteristic peak incidence in March. In the later years there was no well-defined peak but about twice as many cases in the first half of the year as in the second, a form of curve resembling that of the prewar years but two or three times as high, both in winter and in summer. The force of the 1940–42 epidemic did not in fact expend itself until about June, 1947.

ORDINARY FORM

The habitat of the meningococcus is the nasopharynx, where the organism mostly leads a saprophytic or semi-saprophytic existence. Meningococcal infection of the nasopharynx is mainly subclinical. Under exceptional conditions the organism becomes invasive and finds its

* The Milroy lectures to the Royal College of Physicians for 1945. Deferred because of the author's service overseas.

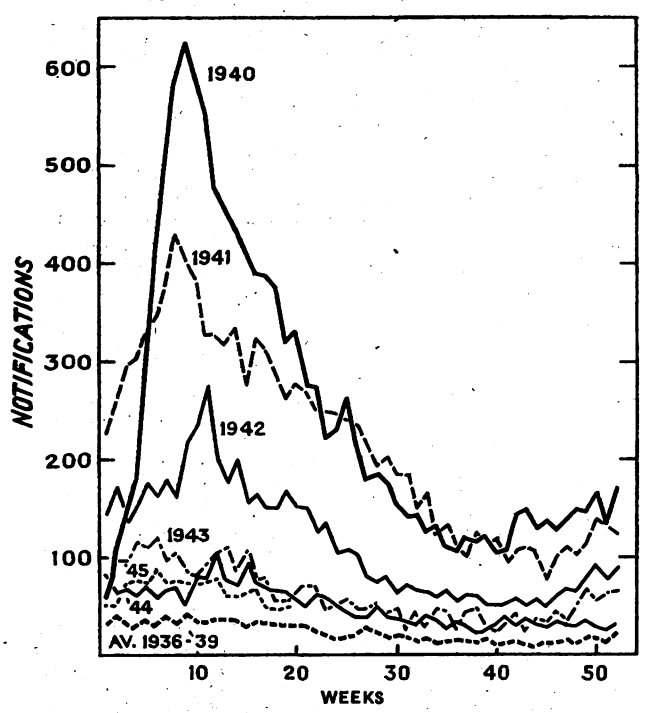


Fig. 1—Weekly notifications of cerebrospinal fever

Digitized by Google

way into the blood-stream and meninges to produce the ordinary form of the disease. This is especially liable to happen with group I strains during an epidemic and with group II strains in infants. Such activity is preceded or accompanied by overt nasopharyngitis in about a third of the cases, but the rôle of the meningococcus in the production of this nasopharyngitis is uncertain, since the common organisms of the upper respiratory tract obscure the picture. A few instances have, however, been recorded of pure cultures of meningococcus in tonsillitis (van Rooyen and Morris 1941), and in nasopharyngitis (Allison 1947). Irrespective of the presence or absence of clinical nasopharyngitis, the same type of organism as that in the spinal fluid may be isolated from the nasopharynx within a day or two of onset of symptoms and it usually then disappears (Flack 1917).

The sequence of events in the ordinary form of the disease is generally held to be: (1) nasopharyngeal infection (usually subclinical); (2) bacteriæmia; and (3) meningitis. Fairbrother (1947) revived the older theory of direct infection of the meninges from the nasopharynx via perineural pathways. This theory is difficult to reconcile, however, with the numerous proved cases of premeningitic meningococcæmia in fulminating and ordinary forms and with ameningitic chronic meningococcal septicæmia. It must be admitted that the exact mechanism by which the organism passes into the blood-stream from the nasopharynx is unknown. Clinical histories and routine blood-cultures suggest that the premeningitic bacteriæmia is usually short—a matter of minutes or hours in the ordinary form. In rare cases it has been observed for two or three days. A papulo-petechial rash is present at this stage in 25–50% of the cases.

The ordinary form is encountered in fully 90% of all clinical cases in epidemic times and probably over 95% in non-epidemic times. It is so well known that it need receive no further attention here. I wish to deal more particularly with the rarer forms of the disease, some of which are less easily recognised and differentiated. Recognition of these syndromes is important in our understanding of the disease, and their early diagnosis is of the utmost importance in treatment.

CHRONIC MENINGOCOCCAL SEPTICÆMIA

Though the chronic septicæmic form was first described as early as 1902 it received little attention until the epidemic of 1940–42, when numerous cases were observed among British troops in France and in the civilian population of Great Britain. It still crops up occasionally, especially in the meningococcal season. It should be borne in mind in all states of intermittent pyrexia accompanied by crops of spots. The clinical picture is usually very characteristic: (1) bouts of pyrexia every two or three days with or without rigors and sweating, sometimes suggesting malaria; (2) recurrent crops of papules, sometimes with petechial centres, on trunk and limbs; (3) raised circular erythematous areas resembling erythema nodosum; and (4) occasional rheumatic accompaniments in the form of pains or swelling of joints, and pains in muscles, tendons, fasciæ, and bones. Priest (1947) described one case with febrile bouts extending over several months in which there was no rash. An attempt should be made to confirm the diagnosis by blood-culture, but this may be negative, even after repeated attempts, in 25–50% of the cases. In pre-sulphonamide days the condition sometimes lasted for months or even years before burning itself out or ending in meningitis. It gets little chance to do so now, for even a few doses of sulphonamides end the condition at once.

ACUTE DIFFUSE ENCEPHALITIC SYNDROME

In severe cases of the ordinary form the patient is often stuporous or semicomatose but resents, and sometimes violently resists, any attempts to treat or disturb him. In contrast with this common clinical picture is the relatively rare development, early in the disease, of deep coma, associated with complete absence of response to gross stimuli, such as pinching and pulling the patient about in bed. Even reflex swallowing may be absent, but this is unusual. Most of these cases resemble the ordinary form for 24 hours or so and then lapse into deep coma suggesting a rapid increase in intracranial pressure. Breathing is laboured or stertorous. Pyramidal involvement is indicated by extensor plantar reflexes and by pareses. A slight papilloedema is common. There is some stiffness of the neck and back associated with the purulent meningitis, but otherwise the muscles may be flaccid. A petechial eruption, usually scanty, may be present, or there may be no rash. Response to sulphonamide treatment is negative or very slow, the condition being often fatal in three to seven days without return of consciousness.

In the absence of any other cause of coma, such as that associated with glycosuria with severe ketonæmia, or concurrent true diabetes, this clinical syndrome is the "acute fatal type" of the older writers. Banks and McCartney (1942) found, in some of these cases, characteristic histological lesions in the brain and cord which might be correlated with the deep coma and other clinical symptoms, and described such cases as the "acute diffuse encephalitic syndrome."

In my series of 706 patients there were 13 considered to belong to this category, of whom 6 recovered and 7 died. Only 4 of the fatal cases could be investigated histologically, but in all 4 the characteristic lesions were found in the brain and cord, varying in degree according to the duration of the comatose state. The lesions consisted not only of congestion and œdema but also of widespread thrombosis in, and hæmorrhage around, small vessels and of perivascular leucocytic infiltration, sometimes with gross deposition of fibrin. Purulent meningitis was always present, but this was usually clearing or had almost cleared as a result of the sulphonamide treatment. In the 2 more protracted cases the perivascular leucocytic infiltration amounted in places to dense zones of polymorphs, suggesting that an abscess was beginning to form. Besides these purely vascular and perivascular lesions there were also degenerative changes in the neurone cells. The lesions were diffusely spread in the brain stem, cerebral hemispheres, cerebellum, and cord (figs. 2–6).

It is somewhat surprising that little confirmatory evidence of this syndrome has, to my knowledge, since been published, except a typical example by Wartman and Hanger (1944), who, using Spielmeyer's myelin stain, showed that the pale areas around the hæmorrhagic foci in the brain were due to displacement of the myelinated nerve-fibres, and that there was no primary demyelination. They point out that the absence of demyelination

LEGENDS TO ILLUSTRATIONS

FIGS. 2 TO 9

Fig. 2—Acute diffuse encephalitic syndrome, 5th day: hæmorrhage and thrombosis with perivascular infiltration in cerebrum. (× 150.)

Fig. 3—Acute diffuse encephalitic syndrome, 5th day: multiple hæmorrhages in cerebrum. (× 140.)

Fig. 4—Acute diffuse encephalitic syndrome, 5th day: thrombosis with perivascular infiltration in cerebrum. (× 290.)

Fig. 5—Acute diffuse encephalitic syndrome, 4th day: thrombosis with polymorph and mononuclear infiltration in cerebrum. (× 610.)

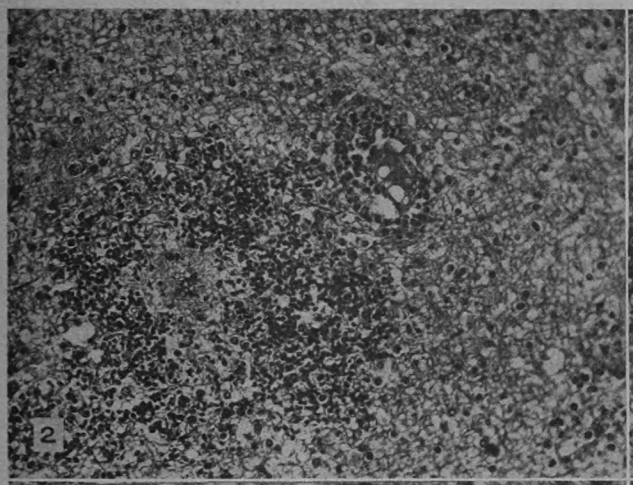
Fig. 6—Acute diffuse encephalitic syndrome, early 3rd day: œdema and thrombosis with early perivascular infiltration in cerebrum. (× 580.)

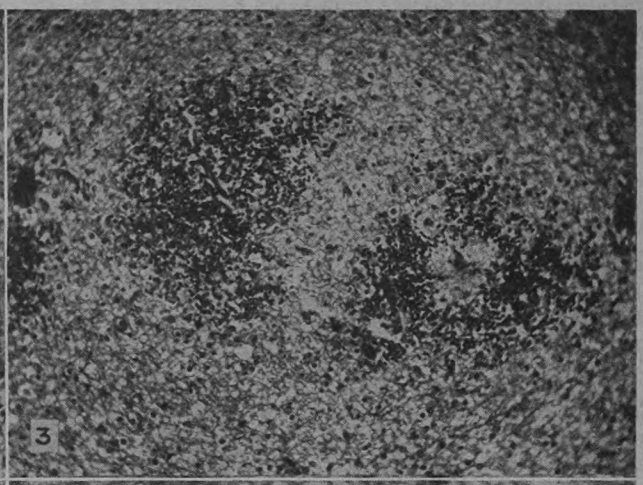
Fig. 7—Fulminating encephalitic syndrome, early 2nd day: thrombosis with commencing perivascular infiltration in cerebrum. (× 400.)

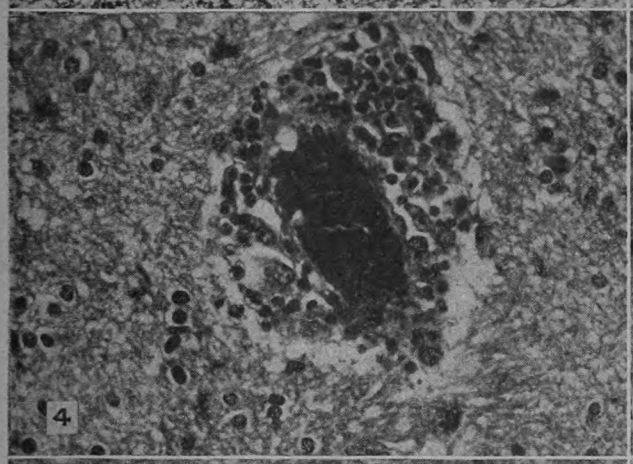
Fig. 8—Fulminating adrenal syndrome: moderate hæmorrhage with necrosis and "tubular lesions" in adrenal cortex. (× 610.)

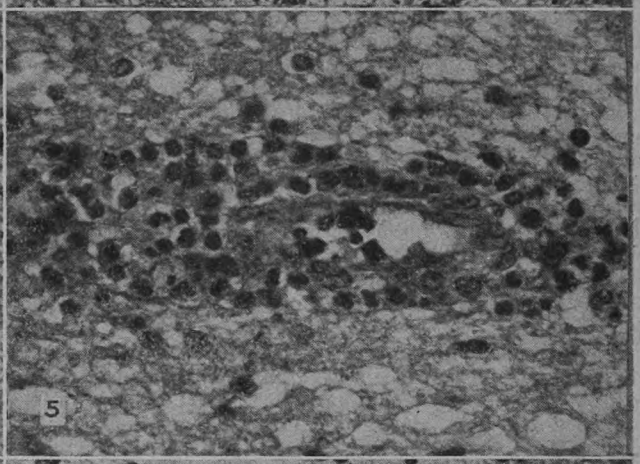
Fig. 9—Acute focal encephalitic syndrome: focal hæmorrhages in midbrain associated with death from subdural hæmorrhage. (× 110.)

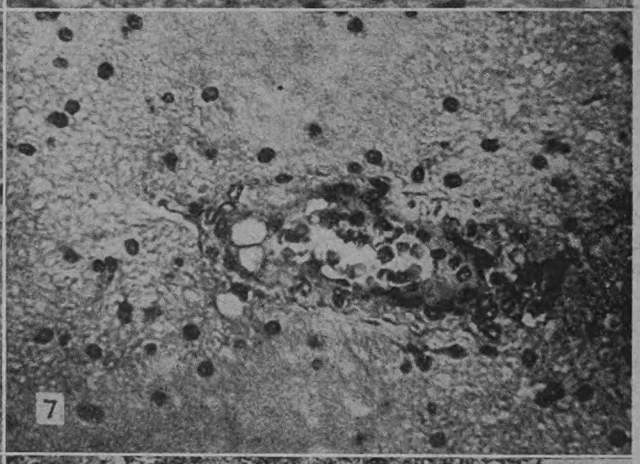
Digitized by Google

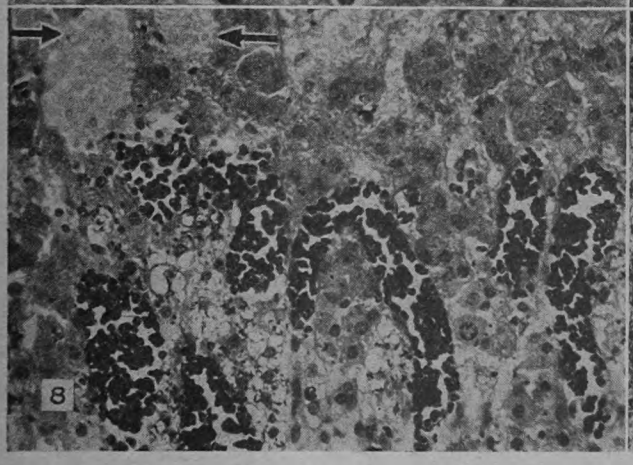












Digitized by Google

distinguishes this disease from acute hæmorrhagic leuco-encephalitis (Baker 1935) and other rare primary demyelinating diseases. Cases can easily be missed at necropsy if the brain and cord are not carefully examined histologically at all levels. I discovered, when I referred back to my pre-1939 cases, that, of 6 cases which clinically might have belonged to this syndrome, brain sections had been preserved only in 1, which on re-examination showed the typical lesion. Photomicrographs of brain sections of the 2 most protracted cases were shown in the original paper (Banks and McCartney 1942). Figs. 2, 3, and 4 show additional brain sections from 1 of these patients, a man of 22 who died on the fifth day of the disease after three days of deep coma. Fig. 5 is a section from another patient, a man of 24 who died on the fourth day of disease.

Though clinicopathological correlation seems fairly clear in such cases, it is naturally less clear in cases that are fatal within three days or less of the onset of the acute illness. I have examined 2 examples of this more acute type in a child of 2 and a man of 45 years. The man died after twenty-five hours' deep coma. The duration of the acute illness was not exactly determined but was probably about forty-eight hours or a little more. In this case sections of cortex, basal ganglia, mid-brain, and medulla all showed diffuse capillary thrombosis, with, here and there, slight perivascular round-celled infiltration limited to a single ring of cells (Banks and McCartney 1942). Fig. 6 is an additional section from this case and shows capillary thrombosis with slight round-cell perivascular infiltration. The lesions here are intermediate between those of the 2 more protracted cases referred to above and those of a fulminating encephalitic case to be described later.

Supporting evidence of the diffuse encephalitic basis of this syndrome is obtainable from recovered patients. In the original paper (Banks and McCartney 1942) we described the case of a girl of 15 with meningococcal meningitis who was in absolute coma for three days and then slowly emerged, becoming rational, but with very slow cerebration, after five days' intensive sulphonamide treatment. During early convalescence she had a mask-like expression, which lasted three weeks. She also had an upper-neurone facial paresis as well as a lower-neurone bilateral sixth-nerve paralysis. The combination of protracted deep coma, transient parkinsonism in convalescence, and upper-neurone involvement, when considered with the pathological data already demonstrated, more than suggests a widespread parenchymatous lesion in the central nervous system.

FULMINATING MENINGOCOCCAL SEPTICÆMIA

Meningococcal septicæmia is sometimes overwhelming and fatal in from as little as four hours from onset to forty-eight hours. Meningitis in such cases is a relatively negligible factor; it is usually absent or just beginning before death or recovery.

It is an old observation that a broad distinction can be drawn clinically between two kinds of fulminating meningococcal septicæmia: that in which the brunt of the onslaught is on the central nervous system, and that in which it is on the peripheral circulation. We have tried to demonstrate a correlation of the first type with the lesions in the brain, minimal as they must be in such a rapidly fatal infection, and of the second type with lesions in the suprarenal glands. We found, however, in a considerable proportion of cases, that both of these systems were involved, giving rise to a mixed clinical syndrome which is confusing, and has actually been confused in the so-called Waterhouse-Friderichsen syndrome (Banks and McCartney 1943).

There are other sources of confusion too in this medley of fulminating meningococcal septicæmia. There is evidence that the pituitary gland is occasionally involved (see below). Again, Morison (1943), on the basis of necropsies on 3 cases with adrenal hæmorrhage, thought that the evidence favoured a generalised vascular lesion leading to peripheral circulatory failure or shock symptoms by the usual mechanism of plasma loss from the circulation. He and others—e.g., Williams (1942)—consider that the lesions in the suprarenals play a relatively insignificant part compared with the general toxic lesions in the production of the symptoms of peripheral circulatory failure. Against this view, however, must be placed many observations indicating that the shock of severe acute infections has a different origin from that associated with trauma or hæmorrhage. Ebert and Stead (1941), for example, showed that the peripheral circulatory failure in 8 cases of severe acute infections was not associated with a decrease in the volume of the plasma or with any other laboratory tests of hæmoconcentration. Moreover, it was not altered by transfusion of plasma or blood. To my knowledge, hæmoconcentration has not actually been demonstrated during life in fulminating meningococcal septicæmia. I shall return to this point again; meanwhile I suggest that sufficient correlation between organic damage and clinical symptoms has been demonstrated to justify the classification of fulminating meningococcal septicæmia into three broad types: (1) encephalitic; (2) adrenal (this might be understood to include occasional pituitary lesions); and (3) mixed or encephalitic-adrenal. Such a classification has at least the advantage of suggesting treatment appropriate to the type.

I deprecate the use of the term "Waterhouse-Friderichsen syndrome" for cases of fulminating septicæmia with massive purpura and bilateral adrenal hæmorrhage, because this syndrome seems to be a composite affair which includes both the "pure adrenal" and the "mixed" syndromes, and so leads to confusion of symptomatology and of treatment. I think it is particularly important to distinguish between cases in which the patients are comatose from an early stage and those in which they are mentally clear. This is not done in the Waterhouse-Friderichsen syndrome, but it is a cardinal distinction in our classification.

(1) *Encephalitic Type*

This is represented by 6 cases in my series of 706 cases of meningococcal disease: 2 in infants, 2 in children of 3 years, and 2 in young adults. All were fatal within forty-eight hours of onset. All of them were acute medical emergencies. Onset was sudden, with anorexia, vomiting, and fever. Lethargy, stupor, and then absolute coma rapidly developed, accompanied by laboured or stertorous breathing. A petechial but not massively purpuric rash appeared within about 12–18 hours of onset, and meningococci were found in the blood. In infants convulsions occurred. The plantar reflexes were extensor. Blood-pressure was normal.

At necropsy the brain was grossly congested and œdematous, and sometimes as much as 50% overweight. Sections at various levels showed early purulent meningitis, and in the parenchyma diffuse capillary thrombosis, small hæmorrhages, and some degeneration of neurone cells. No adrenal or other conspicuous lesion was apparent.

Banks and McCartney (1942) published brain sections from an infant of 11 months who died after thirty-six hours' illness, including ten hours' complete coma. These showed capillary thrombosis, slight perivascular infiltration, and capillary hæmorrhages. Fig. 7 is another section from the same case, showing capillary thrombosis and slight perivascular infiltration. The lesions, as would be expected, are minimal but may be interpreted as a very acute encephalitic basis for the deep coma which is the cardinal sign of fulminating meningococcal septicæmia of the encephalitic type.

Digitized by Google

(2) *Adrenal Type*

This syndrome is represented in the series by 13 patients of whom 8 died and 5 recovered. There were 3 infants under 1 year, 6 children aged 1–6 years, and 4 adults aged 19–34. All 3 infants died, but 4 children and 1 adult recovered. The diagnosis in the recovered cases could, of course, only be presumed from the symptoms.

The main symptoms in this syndrome were a sudden onset of fever, with fretfulness or malaise, and the rapid appearance of a generalised petechial rash, which soon became purpuric. In most cases the purpura became massive, and large cyanotic areas could also be seen in the skin. With the development of purpura, peripheral circulatory failure set in, the blood-pressure being low or unrecordable. Meningococci were present in blood-culture and often in films of the peripheral blood. Signs of meningitis were generally absent on first examination but tended to appear later. In contrast with the encephalitic type the mental state was clear almost to the end. The cardinal signs of the syndrome were the massive purpura, the low blood-pressure, and the clear mental condition, all associated with an overwhelming septicæmia.

At necropsy the brain and meninges showed little more than congestion; the most conspicuous lesions were found in the suprarenal glands—usually bilateral hæmorrhage of various degrees, starting in the inner or reticular layer of the cortex, but often extending inwards to the medulla and outwards almost to the periphery of the cortex, so that much of the gland was destroyed. When the hæmorrhage was massive, some of the large medullary veins might be thrombosed. Many of the cortical cells were out of alignment and showed degenerative changes and even necrosis. This was most easily seen in the actively functioning outer or glomerular layer of the cortex.

Banks and McCartney (1943) published illustrations of various types of hæmorrhagic adrenal lesions, from the earliest stage to massive hæmorrhage accompanied by thrombosis of venus sinuses and complete destruction of the gland. Some of the intermediate types showed not only hæmorrhage but also well-marked degenerative changes in the cortical cells. The same workers, however, also illustrated non-hæmorrhagic adrenal lesions which might be associated with severe adrenal dysfunction. These included gross degeneration of cells of the glomerular cortex with complete disorganisation of the structure of the cortical cords, as well as gross œdema of the whole gland and foci of leucocytic infiltration scattered through the gland. One of these photomicrographs is reproduced here (fig. 8). It shows degeneration and necrosis of cells of the glomerular layer in addition to some hæmorrhage. In this section the "tubular lesions" described by Rich (1944) can also be seen. The solid cords of the cortex have been converted into tubes containing fibrinous exudate from the capillaries as well as much cellular debris. Rich showed that the primary lesion in such cases was necrosis of the hormone-containing cortical cells, and that their death and absorption allowed exudate from the capillaries to flow into the centre of the cortical cords, dissecting them for a variable part of their length into "tubes." Such lesions represent a gross interference with adrenal function and may be present without hæmorrhage.

Another non-hæmorrhagic adrenal lesion is shown in fig. 10. This specimen is from a child of 5 years who died of fulminating meningococcal septicæmia of adrenal type nineteen hours after the appearance of the purpuric eruption. It shows a band of fibrin 3 mm. thick surrounding the gland. This layer of fibrin covered the greater part of both glands. Sections of the suprarenal glands in this case showed only slight hæmorrhage but severe toxic changes in the cortical cells. The thick band of fibrin might have hindered absorption of hormonal secretion.

Such lesions may help to explain those cases which present the signs of fulminating septicæmia of adrenal type, including peripheral circulatory failure during life, but show no adrenal hæmorrhage after death. Absence of gross adrenal hæmorrhage has led some observers—e.g., Williams (1942)—to consider that undue importance has been ascribed to adrenal apoplexy as a cause of the circulatory collapse. It appears, however, that the non-hæmorrhagic microscopic lesions in the suprarenal glands may have been overlooked in some at least of these observations. Kinsman et al. (1946) demonstrated gross degenerative lesions in the cortical cells in 2 cases of this syndrome in which adrenal hæmorrhage was absent. They advanced the theory, based mainly on Rich's work, that the increased demand on the adrenal cells, as a result of the fulminating infection, depletes the cortical cells of lipoid or hormone-containing material. The cells degenerate rapidly, undergo lysis, and shrink, causing loss of support to the capillaries. Up to this point the damage may still be reversible, and efficient chemotherapy of the infection may save the patient. On the other hand, the patient may die from the functional damage or other factors before hæmorrhage takes place. In most fatal cases, however, the cortical capillaries rupture, owing to loss of support and possible weakening of their walls by toxic action. If the resulting hæmorrhage is gross it causes irreversible damage to the gland.

Fig. 10—Fulminating adrenal syndrome: periadrenal thick fibrinous exudate.

This theory seems to indicate at least one important cause of the circulatory failure in fatal cases of the adrenal syndrome in which hæmorrhage is not found, and also in recovered cases. It does not exclude the part played by toxic effects on many other organs and tissues—e.g., heart, vessels, and vasomotor mechanism; but it emphasises and explains the predominant part played by adrenal lesions. The latter include, in some cases, thrombosis of the large medullary venous sinuses along with gross hæmorrhage and necrosis, a condition which has been described as thrombotic necrosis. If the above theory is correct this term would merely describe the end-result and not necessarily the sequence of events, since the cortical necrosis might precede the thrombosis.

In my series all the fatal cases considered clinically to belong to this syndrome revealed hæmorrhagic or non-hæmorrhagic adrenal lesions which might be considered significant. Accordingly, without denying that the general vascular or other toxic lesions may play a part in the production of circulatory collapse, I consider that the correlation of symptoms with adrenal lesions is sufficiently striking to justify designation of this syndrome as "fulminating septicæmia of adrenal type," or, more briefly, "fulminating adrenal syndrome."

(3) *Mixed Encephalitic-adrenal Type*

In this syndrome early deep coma is combined with a purpuric rash and low blood-pressure. At necropsy both the brain and the suprarenals exhibit lesions of the kinds already described for fulminating septicæmia of encephalitic and of adrenal types. In my series there were 5 cases of the mixed syndrome, all fatal: 3 in infants and 2 in children aged 4 and 8 years.

Digitized by Google

TABLE II—VARIETIES OF MENINGOCOCCAL DISEASE IN THE SERIES OF 706 CASES

Variety	No. of cases	Recovered	Died
Ordinary form	647 (91·7%)	632	15
Acute septicæmia only ..	3 (0·4%)	3	..
Chronic septicæmia	3 (0·4%)	3	..
Acute diffuse encephalitic ..	13 (1·8%)	6	7
Fulminating encephalitic ..	6 (0·9%)	..	6
Fulminating adrenal	13 (1·8%)	5	8
Fulminating encephalitic-adrenal (mixed)	5 (0·7%)	..	5
Acute focal encephalitic ..	6 (0·9%)	..	6
Chronic form (hydrocephalus)	10 (1·4%)	5	5
Total	706	654	52

Occasionally, the pituitary gland may be damaged, as in a fatal case clinically corresponding to the mixed syndrome and showing three areas of coagulation necrosis in the pituitary (Gordon and Shimkin 1943). One of my recovered cases of the adrenal type, a child of normal development at the age of 6 years at the time of the illness (Banks and McCartney 1943), was found at the age of 12 to be suffering from the pituitary form of dwarfism. She had grown only 2 inches in the intervening six years and the ossification of certain epiphyses was delayed.

ACUTE FOCAL ENCEPHALITIC SYNDROME

There still remain some fatal cases of meningococcal disease which do not quite fit into any of the above categories. All workers at this subject have been puzzled, at some necropsies, about the precise cause of death. This was expressed by Thomas (1943) in his description of U.S. Army experiences during the war:

> "Out of 46 cases coming to autopsy 18 had gross adrenal hæmorrhage and in most of the remaining cases the cause of death was not clear. The meningitis was cured or subsiding, and death could only be ascribed to toxic action or increased intracranial pressure."

Some of these puzzling cases appear to belong at first to the severe ordinary form, and after a day or two they show signs of recovery. This phase, however, is succeeded by sudden or unexpected collapse, convulsions, or coma and death. In some such cases Banks and McCartney (1942) found focal vascular lesions in the brain stem and the cervical cord. The lesions consisted of isolated focal hæmorrhages, hyaline capillary thrombi, swollen capillary endothelium, and slight perivascular infiltration. Often there was also chromatolysis of nerve-cells. In one case the focal lesion had produced a large subdural hæmorrhage. In some cases these lesions were situated close to the vital medullary centres.

We tentatively suggested that such focal encephalitic lesions might explain some of these unexpected tragedies in which the purulent meningitis had practically subsided at the time of death and could not in itself have caused death. Careful histological examination of necropsy material is necessary for the discovery of most of these focal lesions. There were 6 cases in my series, all fatal—1 infant, 1 child, and 2 young and 2 middle-aged adults. Clinical particulars and brain sections of 2 cases showing focal hæmorrhages have been described (Banks and McCartney 1942). Fig. 9 is a section of the mid-brain from the case of subdural hæmorrhage mentioned above. It shows one large focal hæmorrhage and several smaller ones. Another case in the series was a man of 42 who died on the twelfth day of disease after two successive large cerebral hæmorrhages within twenty-four hours, involving each internal capsule. Up to the ninth day of the disease he had appeared to be a case of the ordinary form.

MILD AND ABORTIVE FORMS

Many cases of mild clinical and subclinical infection undoubtedly occur during an epidemic, especially at the tail end of it. The symptoms include mild pyrexia, headache, stiffness of neck and back, and in abortive cases they may disappear in a day or two without specific treatment. Other mild cases, however, do not clear spontaneously, and the diagnosis may be missed for a week or two, until increasing headache, or continued fretfulness in an infant, compels investigation by lumbar puncture. Such cases may be extremely dangerous owing to slow formation of arachnoid adhesions, with production of hydrocephalus, subarachnoid block, and sometimes compression paraplegia.

CHRONIC FORM

The chronic form is a development of the ordinary form, generally when the latter has been unrecognised or untreated in the early acute stage. It is referred to below. In my series of 706 cases 10 patients had the chronic form, of whom 5 died. This form is now much rarer than it was in the presulphonamide days.

MISCELLANEOUS FORMS

Other rare forms of meningococcosis include primary meningococcal ophthalmia, meningococcal hepatitis, and meningococcal pneumonia. Some 30 cases of the first have been reported, the majority in males so far as is known, under the age of 25 years. It is a primary purulent conjunctivitis involving one or both eyes. Corneal ulceration was noted in about a sixth of the cases. In about a third there was a history of sore throat. In no case was the eye permanently damaged. Meningitis followed in 1 case, and meningococcal septicæmia in 2 (Shuttleworth and Benstead 1947).

A case of meningococcal jaundice was reported by Crawford (1944) in which jaundice appeared twenty-four hours after the onset of a febrile illness and continued for ten days concurrently with meningococcal septicæmia before it was diagnosed by blood-culture and treated with sulphonamides; the temperature then fell to normal in twenty-four hours, and the jaundice disappeared a day later. This case closely resembled Weil's disease, but tests for this were all negative.

A considerable number of cases of meningococcal pneumonia were reported in the first world war in association with the great influenza pandemic (Holm and Davison 1919). In the second world war only one case was reported (Roberg 1945). Subsequently Brick (1948) reported two cases, one of which was complicated by meningococcal empyema. In all these the meningococcus was cultured from the blood or the lung or the sputum, and it was not present in the cerebrospinal fluid.

Table II summarises the varieties of meningococcosis observed in my hospital series of 706 cases and gives their incidence and fatality rates.

(To be concluded)

"... no matter how great the effort, many epileptics will, sooner or later, fail in life's struggle—failure due not to faults of their own but to public ignorance. The enlightenment of public opinion is a tough job. A strong national organisation, with a whole-time staff and adequate funds, could do much to change public opinion; such an organisation would serve the needs of the epileptic in the same way and with the same force as the National Institute for the Blind acts for the blind, the National Institute for the Deaf for the deaf, and the Diabetic Association for the diabetic.... Granted good medical care and a strong national organisation there still remains for epileptics the greatest need of all—regular work."—Dr. PETER HENDERSON, addressing the Royal Institute of Public Health and Hygiene on Oct. 20.

Digitized by Google

INFECTION BY PENICILLIN-RESISTANT STAPHYLOCOCCI

MARY BARBER
M.D. Lond.

MARY ROZWADOWSKA-DOWZENKO
M.D. Warsaw

From the Bacteriology Department, Postgraduate Medical School of London

MANY studies have been carried out on the incidence of penicillin-resistant strains of *Staph. pyogenes* in cases of infection. Until 1944 few such strains were encountered. Since then, however, the incidence has been increasing rapidly, particularly in hospitals. Studies in which more than 10% of all strains tested were found to be resistant to penicillin have been recorded by Spink et al. (1944), Bondi and Dietz (1945), Gallardo (1945), Plough (1945), Harley et al. (1946), Barber (1947a and b), and Simpson (1947). In a previous report one of us (Barber 1947b) showed that in less than a year the incidence of penicillin-resistant strains of *Staph. pyogenes* giving rise to infection in this hospital had gone up from 14·1 to 38%. The work reported here shows that this increase is continuing.

All pus swabs received in the laboratory during this investigation have been plated directly on to plain blood-agar plates and penicillin-ditch plates, the ditch containing 10 units of penicillin per ml. of agar. If other specimens from cases of infection yielded a heavy growth of *Staph. pyogenes*, this growth was emulsified in broth and replated on a penicillin-ditch plate. All staphylococci were tested for coagulase, and only those which were positive were included in the series. If any coagulase-positive staphylococci were shown on the ditch plate to be resistant to penicillin, colonies, usually ten, were picked from a plain blood-agar plate and tested individually for penicillin resistance. All resistant strains isolated were tested for their capacity to destroy penicillin by the method used in the previous studies (Barber 1947a). Sensitivity to streptomycin was tested on ditch plates, the ditch containing 100 units of streptomycin per ml. of agar. Part of every ditch plate used, whether for testing streptomycin or penicillin sensitivity, was seeded with the Oxford staphylococcus as a control.

TABLE I—ANALYSIS OF PATIENTS YIELDING *Staph. pyogenes*

Series	Total patients	Patients with penicillin-resistant strains		
		Total	All colonies tested resistant	Sensitive and resistant colonies isolated
I (April-November, 1946)	99	14 (*14·1%*)	9 (*9·1%*)	5 (*5·1%*
II (February-June, 1947)	100	38	30	8
III (February-June, 1948)	100	59	39	20

ANALYSIS OF RESISTANT STRAINS

Specimens from 100 patients with staphylococcal infection were examined. From 59 patients penicillin-resistant strains of *Staph. pyogenes* were isolated; from 39 all colonies tested were resistant, and from 20 both resistant and sensitive strains were isolated. These results are compared in table I with those of the two previous studies. It will be seen that the incidence of patients yielding penicillin-resistant strains has risen from 14·1% in 1946 to 38% in 1947 and 59% in 1948. In the present series 20 patients gave mixed cultures of penicillin-sensitive and penicillin-resistant strains. In 17 of these patients the mixture was present in a single specimen, and 8 gave only a few penicillin-resistant colonies. From 3 the first specimen received yielded only penicillin-sensitive staphylococci, but from later specimens penicillin-resistant strains were isolated. These 3 patients will be referred to again in connexion with the source of resistant strains. The results according to type of infection were as follows:

Type of infection	*Total patients*	*Patients yielding penicillin-resistant strains*
Septicæmia	2	2
Boils, abscesses, &c.	23	8
Superficial skin lesions	12	8
Infected operation wounds	12	10
Pulmonary	10	7
Conjunctivitis	22	11
Aural	5	3
Nasopharyngeal	6	5
Umbilical of newborn	3	3
Urinary	3	1
Vaginal	2	1
Total	100	59

The 2 patients with septicæmia both died, in spite of intensive penicillin treatment.

One was a newborn infant in whom the infection appeared to enter via the umbilical cord. The infant had had no penicillin before the infection.

The other was a patient with bilateral cortical necrosis of both kidneys following toxæmia of pregnancy and treated with the artificial kidney. Penicillin treatment was started when the patient was put on the artificial kidney, and maintained after the development of septicæmia. Owing to the kidney deficiency a very high blood-penicillin level was reached, but the infecting staphylococcus was so resistant that it was isolated from a blood-culture while the patient was on a dose of penicillin giving levels up to 8 units per ml. of serum. Though the condition of the kidneys would probably have caused death eventually, necropsy revealed septic thrombosis of one iliac vein and the inferior vena cava, septic infarcts throughout both lungs, and one small abscess in the myocardium.

The cases of abscess were of all grades of severity, and the abscesses were in various sites. The superficial skin lesions consisted of ulcers, gangrene, bedsores, burns, dermatitis, and septic spots. The lung infections included pneumonia, bronchiectasis, lung abscess, and tuberculosis. Of the 22 cases of conjunctivitis 20 were neonatal. Of the 5 patients with aural infection, 4 were children with otitis media, and 1 was an adult diabetic with external otitis.

In view of Voureka's (1948) claim that penicillin-resistant staphylococci can be rendered sensitive by growth in the presence of other organisms, whether the latter are sensitive or resistant to penicillin, the strains in this study have been analysed according to whether they were isolated in pure or in mixed culture. The results (table II) show that 34 of the 59 penicillin-resistant strains were originally isolated from 48 mixed cultures, whereas only 25 penicillin-resistant strains were isolated from 52 pure cultures. The large proportion of penicillin-resistant staphylococci isolated from cultures yielding other penicillin-resistant organisms is interesting, but the figures here are too small to be statistically significant.

TABLE II—ASSOCIATION OF *Staph. pyogenes* WITH OTHER ORGANISMS

—	No. of pure cultures	No. of mixed cultures		
		Total	Other bacteria penicillin-sensitive	Some or all other bacteria penicillin-resistant
Total	52	48	27	21
No. yielding penicillin-resistant strains of *Staph. pyogenes*	25 (*48%*)	34 (*71%*)	18	16

Digitized by Google

DEGREE AND TYPE OF RESISTANCE

All the 59 resistant strains produced penicillinase. As has been shown previously (Luria 1946, Barber 1947a), the degree of resistance of such strains when measured in the laboratory may vary many hundredfold according to the size of inoculum used. Therefore no attempt has been made in this study to estimate the exact amount of penicillin which would inhibit growth. It may be said, however, of all the strains that if a single colony was streaked across a penicillin-ditch plate containing 10 units of penicillin per ml. of agar in the ditch, growth took place right across the plate. Strains showing a minor degree of resistance were not encountered. One interesting phenomenon shown by these penicillin-destroying staphylococci was that colonies in the neighbourhood of the ditch were just as large as those elsewhere. Where the inoculum was small, growth of such organisms might be completely inhibited by the penicillin in the ditch; but if growth did take place it was apparently unimpeded. This is in striking contrast to the growth of a penicillin-sensitive staphylococcus, which usually shows progressively smaller colonies as the ditch is approached.

STREPTOMYCIN SENSITIVITY

Streptomycin-sensitivity was tested in 97 strains: 55 were penicillin-resistant; 13 were penicillin-sensitive strains isolated in association with 13 of the resistant cultures; and 29 were penicillin-sensitive strains isolated from patients who yielded no penicillin-resistant colonies. Broth-cultures of the organism were plated on to streptomycin-ditch plates opposite a culture of the Oxford staphylococcus. All 42 penicillin-sensitive and 53 of the 55 penicillin-resistant strains showed a sensitivity to streptomycin similar to that of the Oxford staphylococcus; one penicillin-resistant strain showed a few resistant colonies when the broth-culture was plated on a streptomycin-ditch plate, but 50 colonies picked from a plain blood-agar plate and streaked across a streptomycin-ditch plate all showed a sensitivity similar to that of the Oxford staphylococcus; from one penicillin-resistant strain all colonies tested appeared to be considerably more resistant than the Oxford staphylococcus to streptomycin.

SOURCE OF RESISTANT STRAINS

It is not disputed that the rapid increase of penicillin-resistant staphylococci is primarily caused by the widespread use of penicillin. There are, however, at least two ways in which penicillin may have this effect. Either a strain may acquire resistance to penicillin, or naturally resistant organisms, originally few, may survive while penicillin-sensitive organisms are destroyed, and thus by a simple process of selection become increasingly common. In an attempt to find out whether one or both of these processes is taking place, the results here recorded have been studied in relation to penicillin treatment and epidemiology. Selected groups of staphylococci were kindly phage typed by Dr. Allison.

The penicillin sensitivity of *Staph. pyogenes* in relation to previous recent treatment with penicillin was as follows:

	Penicillin	*No penicillin*
Penicillin-sensitive strains only ..	4	37
Penicillin-resistant strains isolated	29	30

Only 4 patients who had had penicillin before the swab was taken yielded penicillin-sensitive staphylococci, and 2 of these 4 had only been treated for a day, and 1 only for two days. On the other hand, 30 patients who had not had penicillin recently before the swab was taken yielded penicillin-resistant strains. Of these 30 patients 1 had had a course of penicillin injections three months previously, but no history of penicillin treatment at any time was obtained from the remaining 29. It is interesting, however, that 21 of this group of patients were in the maternity department, 19 having neonatal infections.

As stated previously, from 3 patients (cases 1, 2, and 3) the first specimens tested yielded staphylococci which were all as sensitive as the Oxford staphylococcus to penicillin, but subsequent specimens revealed the presence of penicillin-resistant staphylococci.

CASE 1 had empyema, and the first specimen of pus examined was taken after a three-week course of penicillin injections (30,000 units three-hourly). This gave a growth of penicillin-resistant *Ps. pyocyanea* and penicillin-sensitive *Staph. pyogenes*. Three weeks later a second specimen yielded *Proteus*, *Ps. pyocyanea*, and a few colonies of *Staph. pyogenes*, all of which were penicillin-resistant.

CASE 2 had an abscess in each axilla. A specimen of pus from the right axilla, taken on March 8, gave a pure growth of *Staph. pyogenes*, all of which appeared as sensitive as the Oxford staphylococcus to penicillin. Penicillin treatment, 60,000 units six-hourly, was started, and specimens of pus taken next day from both axillæ yielded pure growths of *Staph. pyogenes*, but the specimen from the right axilla showed a few penicillin-resistant colonies. A penicillin-sensitive colony from each of the three specimens and one of the penicillin-resistant colonies were all subcultured and sent to Dr. Allison for phage typing. The phage reactions were as follows:

Source of specimen	*Date of specimen*	*Penicillin-sensitive colonies*	*Penicillin-resistant colonies*
Right axilla ..	March 8 ..	42 E ..	—
,, ,, ..	,, 9 ..	42 E ..	6/47
Left' ,, ..	,, 9 ..	42 E ..	—

It will be seen that the three penicillin-sensitive colonies were of the same phage type, whereas the resistant colony was different.

CASE 3 had bronchopneumonia and bronchiectasis. His sputum on admission gave a pure growth of penicillin-sensitive *Staph. pyogenes*. Four days later, after 24 hours' penicillin treatment (30,000 units three-hourly), a second specimen gave a similar pure growth of *Staph. pyogenes*, but of 20 colonies tested against penicillin 19 were resistant and 1 was as sensitive as the Oxford staphylococcus. Sensitive and resistant colonies were phage typed as follows:

Date of specimen	*Penicillin-sensitive colonies*	*Penicillin-resistant colonies*
7/5	52	—
11/5	44A (w) ..	47 (+)

(w) = weak. (+) = side reactions.

Here it is seen that all 3 colonies tested were of different phage types.

CASE 4, in contrast to cases 2 and 3, had an infected operation wound which gave a mixed flora of *Proteus* and *Staph. pyogenes*; 10 of the staphylococcal colonies from this case were tested against penicillin, and 9 were found resistant and 1 sensitive. A sensitive and a resistant colony were phage typed, and both gave the reaction 47 (+).

Of the patients studied, 17 came from the two main surgical wards, and 13 of these yielded penicillin-resistant strains of *Staph. pyogenes*. In 10 of the patients the organisms were isolated from infected operation wounds, and from 9 of these 10 patients penicillin-resistant strains were isolated. The noses and skin of 21 members of the staff working in these wards were therefore tested for

TABLE III—CARRIER-RATE OF *Staph. pyogenes* IN STAFF OF SURGICAL WARDS

Site	*Staph. pyogenes* not isolated	*Staph. pyogenes* isolated		
		Total	Penicillin-sensitive only	Penicillin-reisstant colonies isolated
Total ..	12	9	3	6
Nose ..	..	8	3	5
Skin ..	..	2	1	1

Digitized by Google

the presence of similar organisms. The results are given in table III.

Penicillin-resistant strains of *Staph. pyogenes* were isolated from 2 surgeons and 4 nurses; from 4 of the 6 all colonies of *Staph. pyogenes* isolated appeared to be penicillin-resistant, and from 2 resistant and sensitive colonies were isolated. Penicillin-resistant colonies from all these 6 members of the staff, from the 9 cases of operation wounds infected with penicillin-resistant strains of *Staph. pyogenes*, and from one patient with a similarly infected burn were phage typed as follows:

Source	Date of isolation	Phage reaction
Infected wound 1	March 3	47 (+)
,, ,, 2	Feb. 23	47 (+)
,, ,, 3	,, 26	47 (+)
,, ,, 4	March 3	47 (+)
,, ,, 5	April 12	6/47 (+)
,, ,, 6	,, 20	47 (+)
,, ,, 7	,, 19	47 (+)
,, ,, 8	,, 19	47 (+)
,, ,, 9	May 7	47 (+)
,, burn	April 27	6/47 (+)
Surgeon 1 Skin	March 31	6/47 (+)
,, 2 Nose	April 24	3B/3C/51
Nurse 1 Nose	March 31	N.T.
,, 2 ,,	April 3	42B/42E/47C
,, 3 ,,	March 31	N.T.
,, 4 ,,	,, 31	47 (+)

(+) = side reactions. N.T. = not typable.

It will be seen that 8 of the 10 patients were infected by staphylococci of the same phage type, 47 (+), and that one nurse carried this type in her nose. The strains from the other 2 patients were both 6/47 (+), and this phage type was present on the skin of one surgeon. What, however, is rather surprising is that at least 3 other penicillin-resistant phage types were present in the noses of members of the staff.

Previously it had been found (Barber 1947b) that the proportion of penicillin-resistant staphylococci in the maternity department was 56% while that of the rest of the hospital was 38%. It had also been shown that 5 infections with such strains in this department in six weeks were all due to organisms of phage type 6/47. It had been shown that *Staph. pyogenes* of this phage type was present in the air of 2 of the maternity wards at about the same time. Since then precautions had been taken in this department to guard against cross-infection, and all prophylactic penicillin had been stopped. In the present series 31 cases came from maternity wards, and 17 (55%) of them were due to penicillin-resistant organisms.

DISCUSSION

Three important questions arise in connexion with these penicillin-resistant strains of *Staph. pyogenes*, and at present no satisfactory answer can be given to any of them.

1. How do these strains arise? Before attempting to deal with the more fundamental aspect of this question I think it should be stated that, though penicillin-resistant strains of *Staph. pyogenes* are now appearing with increasing frequency in many hospitals, this is probably not the case in the community at large. Harley et al. (1946) showed that the percentage incidence of penicillin-resistant strains of *Staph. pyogenes* as hospital infections in wounds was nearly double that of the percentage in all infections. This would be expected. The frequency of cross-infection in hospitals has been emphasised by many workers (see Miles et al. 1940, Allison et al. 1946). Gillespie et al. (1939) showed that up to 40% of the hospital staff might carry *Staph. pyogenes*, and this has since been confirmed repeatedly. That these human carriers often give rise to hospital infections is not now disputed, and they, together with cross-infection from patient to patient, are probably the ultimate cause of all such cases (Hare and Mackenzie 1946). It is equally possible that a member of the staff may become a nasal carrier of a particular strain of staphylococcus as a result of infection from a patient. Thus it is possible that the number of strains of staphylococci in infections in a particular hospital at any one time may be quite small, and once a penicillin-resistant strain appears it will survive while penicillin-sensitive strains are rapidly eliminated by penicillin. Thus by a simple process of selection penicillin-resistant staphylococci may come to outnumber penicillin-sensitive strains. That this process of selection is taking place is clear from the phage reactions listed above, and from the fact that a similar group of infections in one department in the 1947 series were all caused by penicillin-resistant staphylococci of the same phage type.

Is this process of selection the whole story? Or are these penicillin-resistant strains organisms which were naturally sensitive to penicillin but at some stage in their career acquired resistance to it? The former hypothesis is supported by cases 2 and 3, who yielded penicillin-sensitive and penicillin-resistant strains of unrelated phage types. A similar case was reported in the series studied between February and June, 1947 (Barber 1947b), and 5 such cases in the series of April-November, 1946 (Barber 1947a). On the other hand, case 4 of the present series and a patient in the 1946 series had penicillin-sensitive and penicillin-resistant organisms of the same phage type, and North and Christie (1946) have reported a case where a single serological type of *Staph. pyogenes* appeared to develop resistance under treatment.

One objection to the view that these strains acquire their resistance is that it has not so far been possible to train a staphylococcus in vitro to destroy penicillin. The type of resistance to penicillin produced in the test-tube is quite different. Whether or not, however, these penicillinase-producing staphylococci acquire their resistance, as indicated above selection probably plays a large part in the increasing frequency of their appearance.

2. Can infections with these organisms be successfully combated with massive doses of penicillin? It appears that they can in some cases. The determining factor is probably the heaviness of the infection. These staphylococci are resistant to penicillin largely because they destroy it; a large inoculum has enough ready-made penicillinase to grow in 1000 units of penicillin per ml., whereas a small inoculum may be inhibited by less than 1 unit per ml.

3. Is it possible to make these resistant organisms sensitive to penicillin? Both Voureka (1948) and Winner (1948) claim that this can be done by growing them in mixed cultures. We have been unable to confirm this. I have pointed out (Barber 1948) that strains which have been kept in the laboratory for some time do not breed true but tend to give rise to increasing numbers of penicillin-sensitive daughter colonies; and that after growing ten strains in the presence of the Milne streptococcus, which was one of the organisms used by Voureka, there was no significant increase in the number of penicillin-sensitive colonies. Voureka (1948) started her work with the suggestion that penicillin-resistant organisms might lack some chemical factor which other bacteria might supply, thus rendering the resistant organisms sensitive to penicillin. She does not differentiate clearly in her paper between staphylococci which have acquired resistance in vitro and penicillinase-producing strains. Whatever may be the case with the former, it seems clear that the latter do not lack anything but, on the contrary, have an extra property—the capacity to destroy penicillin. They show none of the morphological, cultural, and pathogenic differences seen in staphylococci which have acquired resistance in vitro. Voureka's claim that the same process renders both types of resistant organism sensitive seems unlikely. However, since penicillinase-producing staphylococci do not breed true, it seems possible that the

Digitized by Google

natural tendency of the organisms to produce penicillin-sensitive daughter colonies might be accelerated by artificial means. Further research along these lines is clearly needed.

SUMMARY

Of 100 cases of infection with *Staph. pyogenes* investigated in one hospital between April and June, 1948, 59 yielded penicillin-resistant organisms. Previous studies in the same hospital gave an incidence of 14·1% in 1946 and 38% in 1947.

The 59 resistant strains have been analysed according to type of infection and whether they were isolated in pure or mixed culture.

All 59 produced penicillinase and when tested by streaking a single colony across a penicillin-ditch plate were resistant to at least 10 units of penicillin per ml.

The incidence of resistant strains has been studied in relation to penicillin treatment and epidemiology in an attempt to throw light on their source. It is suggested that a process of selection is the major factor for their increasing incidence in hospitals.

Our thanks are due to Dr. V. D. Allison for the phage typing results and to Dr. E. Cooper, Dr. J. Holborow, and Dr. D. Mitchison for the primary isolation of many of the strains.

REFERENCES

Allison, V. D., Bourdillon, R. B., Craig, W. S., Crooks, J., Crosbie, W., Gaisford, W., Gunn, W., Lightwood, R., Spence, J. C., Vining, C. W., Watkins, A. G. (1946) *Brit. med. J.* i, 673.
Barber, M. (1947a) *J. Path. Bact.* **59**, 373.
— (1947b) *Brit. med J.* ii, 863.
— (1948) *Lancet*, i, 730.
Bondi, A. jun., Dietz, C. C. (1945) *Proc. Soc. exp. Biol., N.Y.* **60**, 55.
Gallardo, E. (1945) *War Med.* **7**, 100.
Gillespie, E. H., Devenish, E. A., Cowan, S. J. (1939) *Lancet*, ii, 870.
Hare, R., Mackenzie, D. M. (1946) *Brit. med. J.* i, 865.
Harley, H. R. S., Baty, J. A., Bowie, J. H. (1946) *Ibid*, p. 639.
Luria, S. E. (1946) *Proc. Soc. exp. Biol.. N.Y.* **61**, 46.
Miles, A. A., Schwabacher, H., Cunliffe, A. C., Ross, J. P., Spooner, E. T. C., Pilcher, R. S., Wright, J. (1940) *Brit. med. J.* ii, 855.
North, E. A., Christie, R. (1946). *Med. J. Aust.* i, 176.
Plough, H. H. (1945) *Amer. J. clin. Path.* **15**, 446.
Simpson, J. S. (1947) *Bull. Inst. med. Lab. Tech.* **13**, 81.
Spink, W. W., Ferris, V., Vivino, J. J. (1944) *Proc. Soc. exp. Biol., N.Y.* **55**, 207.
Voureka, A. (1948) *Lancet*, i, 62.
Winner, H. I. (1948) *Ibid*, p. 674.

CAROTID-SINUS SYNDROME

A CASE TREATED BY BILATERAL DENERVATION

RICHARD TURNER
O.B.E., M.D. Camb., M.R.C.P.
SENIOR LECTURER IN MEDICINE

J. R. LEARMONTH
C.B.E., Ch.M. Glasg., F.R.C.S.E.
REGIUS PROFESSOR OF CLINICAL SURGERY AND PROFESSOR OF SURGERY
UNIVERSITY OF EDINBURGH
From the Western General Hospital and the Royal Infirmary, Edinburgh

Hering (1927) discovered the mechanism in animals through which pressure over the carotid sinus leads to slowing of the heart, by demonstrating sensory nerve-endings in the wall of the artery and tracing afferent nervous connexions with the medulla. These observations were confirmed by Heymans (1929) and later workers. It is now established that afferent impulses, arising as a result of stimulation of receptor organs in the adventitia of the carotid sinus and aortic arch by changes in intra-arterial pressure, normally play a part in the reflex regulation of blood-pressure and heart-rate; the centre for the reflex is in the medulla. An increase in intracarotid pressure is followed by a reduction in the systemic blood-pressure and in the heart-rate; a decrease has the opposite effect. The reflex is most active when the change in intracarotid pressure is sudden. It is present in man, and most marked in hypertensive persons.

The clinical implications of these observations were studied in detail by Weiss and Baker (1933), Ferris et al. (1935), and Weiss et al. (1936), who showed that hypersensitivity of the carotid-sinus reflex might be responsible for some cases of syncope and of convulsions, and such lesser disorders of cerebral function as dizziness and weakness. The patient is usually a middle-aged or elderly man, often with arteriosclerosis, hypertension, and emotional instability. Symptoms may be precipitated by a sudden movement of the neck, may appear without warning, or may be preceded by an aura such as weakness, dizziness, or epigastric discomfort. At the onset of an attack the patient is usually standing or sitting, and further symptoms, such as loss of consciousness, may be prevented by lying down immediately.

Three types of attack were described, depending on the dominant motor pathway of the hypersensitive reflex:

(1) *Vagal.*—Cardiac arrest from sino-auricular or auriculo-ventricular block, leading to cerebral anoxæmia and a fall in blood-pressure. This can be abolished with atropine and prevented with adrenaline through its local stimulating effect on the ventricules.

(2) *Depressor.*—Reflex vasodilatation with a fall in blood-pressure and cerebral anoxæmia, the least common type. This can be aborted or prevented with adrenaline but not abolished with atropine.

(3) *Cerebral.*—No change in heart-rate or blood-pressure, but stimulation of cerebral centres as a result of impulses reaching the medulla. This is not affected either by atropine or by adrenaline.

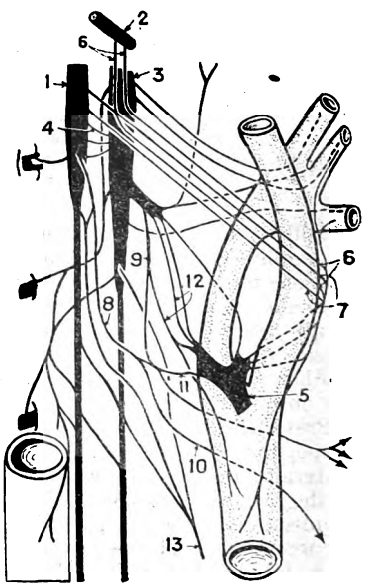


Fig. 1—Posterior view of nerve connexions of carotid body: 1, vagus nerve; 2, glossopharyngeal nerve; 3, superior cervical sympathetic ganglion; 4, anastomotic branch; 5, carotid body; 6, glossopharyngeal pedicle; 7, vagal lateral pedicle; 8, superior laryngeal nerve; 9, sympathetic root of superior laryngeal nerve; 10, lateral branch of superior laryngeal nerve; 11, vagal medial pedicle; 12, sympathetic pedicle; 13, superior cardiac nerve.

Mixed forms may occur. Naturally such attacks cause nervousness and anxiety. The important diagnostic point which distinguishes them from other conditions, such as epilepsy, is their constant reproduction by pressure over one or other carotid sinus.

If the attacks are mild and not seriously incapacitating, reassurance, and the administration of sedatives and ephedrine may be all that is necessary; but, if they are severe and recurrent and there is no response to simpler measures, denervation of the carotid sinus on one or both sides is indicated, a procedure shown by Weiss et al. (1936) to abolish the reflex. Examples of successful unilateral denervation have been reported.

It has been shown that unilateral carotid-sinus denervation has no permanent ill effects (Craig and Smith 1939, Mulholland and Rovenstine 1941, Ray and Stewart 1942), but reports on bilateral denervation are few, at least in English publications, and this operation seems seldom to have been performed, presumably through fear of untoward after effects. Capps and de Takats (1938) re-investigated two patients on whom this procedure had been carried out apparently for epilepsy and found that neither hypertension nor tachycardia had resulted; but postural hypotension was considerable.

Digitized by Google

Fig. 2—Anteroposterior view of chest, showing prominent aorta.

Fig. 3—Left oblique view of chest, showing uncoiled and atheromatous aorta, and left ventricle not enlarged.

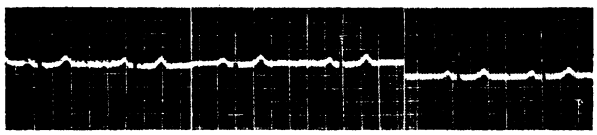
Craig and Smith (1939) described one case in a man of 48, in which improvement did not follow bilateral denervation; however, few details are given and, though they state that both sinuses were hypersensitive, they do not mention whether the attacks could be reproduced by pressure over them.

ANATOMY OF NERVES OF CAROTID SINUS

The nerves of the carotid sinus are disposed in three groups or pedicles, derived from the glossopharyngeal nerve, the vagus nerve, and sympathetic nerves (fig. 1).

(1) *From the Glossopharyngeal Nerve.*—At the point where the glossopharyngeal nerve crosses the lateral aspect of the internal carotid artery it gives off two branches which descend on the lateral aspect of the artery, pass towards its anterior aspect, and end in the anterior border of the carotid body.

(2) *From the Vagus Nerve.*—The vagus nerve supplies a lateral and a medial set of branches. The lateral branches arise from the trunk of the nerve or from the ganglion nodosum. They follow the same course as the glossopharyngeal pedicle, with which they are intimately related. The medial (and more important) branches first run with the superior laryngeal and pharyngeal branches of the vagus; leaving these, they pass to the posterior aspect of the internal carotid artery to end in the posterior border of the carotid body.



Lead I Lead II Lead III

Fig. 4—Electrocardiogram.

(3) *From Sympathetic Nerves.*—Numerous fibres spring from the superior cervical ganglion and the pharyngeal plexus, run in contact with the posterior aspect of the internal carotid artery, and end (above the nerves of the vagal pedicle) in the posterior border of the carotid body. Occasionally a twig reaches the carotid body from the hypoglossal nerve.

CASE-RECORD

The following is an example of the vagal type, apparently cured by bilateral carotid-sinus denervation, without any adverse after effects.

A retired banker, aged 61, was admitted as an emergency on Dec. 10, 1946, after a sudden attack of giddiness and vomiting.

Past History.—About 15 years ago, while sitting at his office desk, he had an attack of weakness in which his head fell back suddenly two or three times, for no accountable reason, and he was off work for several weeks. For the past 12 years or so, he had had "giddy turns," consisting of the sudden onset of a sensation of falling to one side or the other, with a swaying or staggering gait. The first attack came on while he was playing golf; other attacks have occurred when turning quickly, looking up—e.g., at a bookshelf—moving his head to one side or the other, and sometimes while sitting still at his desk. There is no warning of an attack, and he has never lost consciousness. The attacks have gradually become more frequent but are usually of a similar severity and last about 10 minutes. Once he wanted to get out of bed in the night and, turning on his left elbow, fell suddenly and violently backwards. This happened five or six times until he felt faint and sick.

He has been under the care of his doctor, who has called about once a month, and records of the blood-pressure have been kept: from December, 1945, the readings have been 160–200/110–115 mm. Hg.

a Lead III b

Fig. 5—Cardiac asystole caused by pressure over right carotid sinus: *a*, pressure applied; *b*, pressure released.

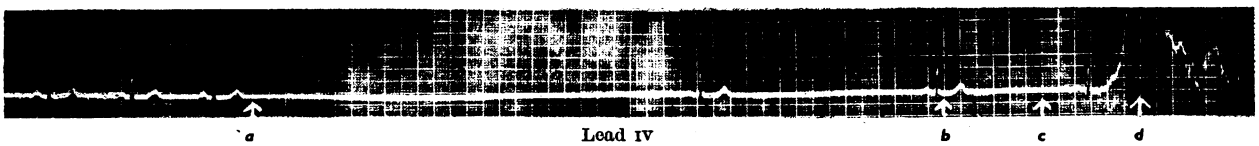
The patient has occasionally noted "blind spots," usually associated with his attacks but sometimes not, consisting of a black area about 10 cm. wide, outlined by a quivering margin, on the page which he is reading. Apart from minor disorders, he has otherwise been well; but he had a nervous breakdown in 1914, benign "glycosuria" in 1925, and his doctor has always thought some of his symptoms were of nervous origin. The patient recently retired from business. A labyrinthine cause for the attacks has been excluded.

Family History.—His father was an asthmatic and died of Bright's disease at 66. His mother died at his birth.

Present Illness.—On the day of admission the patient experienced temporary giddiness when he got out of a tram-car and turned suddenly to cross the road. He went into a restaurant and began his lunch. Again he felt sick, with sweating and water-brash, got up, and staggered to the cloakroom, where he was violently sick and collapsed.

On Admission.—General condition good. High-coloured with clinical polycythæmia. Still feeling cold after his attack but well oriented and not collapsed. Heart not clinically enlarged. No abnormality on auscultation. Blood-pressure 220/130 mm. Hg, with a silent gap between 210 and 160 mm. Pulse regular, rate 80 per min.; mild retinal arteriosclerosis. Other systems normal.

Radiography.—Left ventricle not enlarged. Cardiac outline normal. No hilar congestion. Aorta somewhat uncoiled, elongated, and dense, suggesting atheroma (figs. 2 and 3).



a Lead IV b c d

Fig. 6—Effect of pressure over left carotid sinus: *a*, pressure applied; *b*, loss of consciousness; *c*, convulsion; *d*, pressure released.

Digitized by Google

Urine.—Sp. gr. 1·028. No albumin or sugar. Microscopically normal.

Blood.—Red cells 6,200,000 per c.mm., Hb 120%, white cells 11,200 per c.mm. Blood-urea nitrogen, 18 mg. 100 ml. Wassermann reaction negative.

Electrocardiogram.—Normal limb leads (fig. 4) and chest leads.

Progress.—In view of the failure to find any other abnormality, and the presence of polycythæmia and symptoms probably related to hypertension, venesection 600 ml. was performed on Dec. 15. On Dec. 22, shortly before his discharge, he sat up in bed to look down at his breakfast tray, and this precipitated one of his attacks, an event which suggested that his symptoms might be due to a hypersensitive carotid sinus.

This was easily confirmed by light pressure over either carotid sinus which produced immediate cardiac asystole (fig. 5), and symptoms similar to those to which he is accustomed in his attacks immediately followed. The left carotid sinus was more sensitive than the right. Pressure on the left side was then made and kept up while a continuous electrocardiogram was taken. Immediate cardiac asystole was again produced; in 9 seconds he lost consciousness, and in 10 seconds began a generalised convulsion, whereupon the pressure was released (fig. 6).

The patient seemed to be sensible, if somewhat sensitive, and though he had retired from business his whole life was being seriously inconvenienced by these attacks, which were also a source of anxiety and uncertainty. Bilateral denervation of the carotid sinus was recommended.

Since both carotid sinuses were so extremely sensitive, it was thought advisable to expose each in turn, and to anæsthetise it, before proceeding with the stripping, so as to avoid any disturbance consequent on the manipulation of the vessels which would be required.

Operation (Jan. 16, 1947).—Dr. John Gillies gave thiopentone and cyclopropane; Mr. A. J. Slessor assisted. The bifurcation of the right common carotid artery was freely exposed through an incision along the anterior border of the sternomastoid, and the three vessels were covered with a swab soaked in 2% procaine solution. A similar procedure was next carried out on the left side. When, after 10 minutes, the operation on the right side was resumed, firm pressure on the carotid sinus did not give the abnormal response. The vessels were rigid from calcareous changes. Some 2% procaine was injected under the adventitia of the common, internal, and external carotid arteries for a length of 5 cm., after which the adventitia was removed by sharp dissection. On the left side the findings and procedure were the same. The wounds were closed without drainage, and the patient's convalescence was uneventful.

Follow-up in Outpatients' Department.—On Feb. 5, 1947 (20 days after operation), there had been no further attacks similar to his previous experiences, but a few short attacks of palpitation, coming on suddenly, lasting for a few minutes, and apparently slowly passing off had been experienced. It was considered possible that these were brief attacks of paroxysmal tachycardia, but were more probably simple sinus tachycardia. The patient had also had one attack of loss of vision for the central part of a page. This was the first for over a year and was considered to be due to vasospasm. General condition good. Heart clinically normal. Blood-pressure 210/120 mm. Hg. No change in the rate or volume of the pulse when either carotid sinus was pressed firmly.

March 5, 1947: No further attacks, but on several occasions has had a light feeling in the head as though falling through the air, accompanied by weakness of the legs but no faintness or dizziness, and lasting about 10 minutes—quite unlike his previous attacks. Blood-pressure 150/100 mm. Hg. He has been taking 'Theominal.'

April 16: Two weeks ago had an attack of "acute gastritis," when his doctor found a blood-pressure of 130/85 mm. Hg. Also had two brief attacks of central loss of vision. Blood-pressure 180/110 mm. Hg. Firm pressure over either carotid sinus has no effect on the pulse.

May 28: Quite well. Playing golf. Blood-pressure 170/105 mm. Hg.

July 9: Very well. No recurrence of symptoms after the operation six months ago. Blood-pressure 180/120 mm. Hg. Screening of heart showed no change from previous examination. Electrocardiogram normal.

Oct. 1: Very well. Blood-pressure 180/110 mm. Hg.

Jan. 14, 1948: No complaints. No recurrence of his attacks. Now that his confidence has been restored he is leading a normal life and playing golf regularly. No symptoms of postural hypotension. Heart clinically normal. Radiography as before. Blood-pressure 190/110 mm. Hg. Firm pressure over either carotid sinus has no effect.

On April 28, when last seen, he reported two momentary attacks of giddiness, unlike those experienced before, but associated with a similar area of loss of vision in one eye. One attack occurred while walking down the main road and another while playing golf, but neither was sufficiently severe to interfere with what he was doing. Physical findings were as before, and, since there has been no return of the sensitivity of either carotid sinus, it may well be that these two brief attacks of giddiness, accompanied by scotomata, were associated with vasospasm and related to his hypertension.

SUMMARY

A man of 61 with benign essential hypertension had frequent incapacitating attacks of giddiness, which were shown to be due to hypersensitive carotid-sinus reflexes.

Bilateral carotid-sinus denervation was carried out, and during the succeeding year the patient has been free from his previous attacks. There have been no adverse effects from the operation.

The possibility of this ætiology should be considered in similar cases.

REFERENCES

Capps, R. B., de Takats, G. (1938) *J. clin. Invest.* **17**, 385.
Craig, W. M., Smith, H. L. (1939) *Yale J. Biol. Med.* **11**, 415.
Ferris, E. B. jun., Capps, R. B., Weiss, S. (1935) *Medicine*, **14**, 377.
Hering, H. E. (1927) Die Karotissinusreflexe auf Herz und Gefässe. Dresden.
Heymans, C. (1929) Le sinus carotidien et les autres zones vasosensibles réflexogènes. Paris.
Mulholland, J. H., Rovenstine, E. A. (1941) *Surgery*, **9**, 751.
Ray, B. S., Stewart, H. J. (1942) *Ibid*, **11**, 915.
Weiss, S., Baker, J. P. (1933) *Medicine*, **12**, 297.
— Capps, R. B., Ferris, E. B. jun., Munro, D. (1936) *Arch. intern. Med.* **58**, 407.

FATAL STAPHYLOCOCCAL ENTERITIS DEVELOPING DURING STREPTOMYCIN THERAPY BY MOUTH

IVOR R. H. KRAMER
L.D.S. R.C.S.
ASSISTANT PATHOLOGIST, PRINCESS LOUISE CHILDRENS UNIT, ST. MARY'S HOSPITAL, LONDON

IT has been shown (Elias and Durso 1945, James and Kramer 1948) that when streptomycin is administered by mouth extremely high concentrations of the drug may be obtained in the stools (up to 9000 units per g.), and the growth of any sensitive organisms already present or passing through the stomach during oral streptomycin therapy would be effectively prevented. Recently (James and Kramer 1948) attention has been drawn to the possibility that, in patients receiving streptomycin by mouth, organisms remote from the gut may be rendered resistant by the small amount of the drug entering the blood-stream. This mechanism may provide a focus of resistant pathogens capable of reaching the gut and multiplying there, particularly in infants, where the bactericidal action of the gastric secretions is less than in the adult. It seems probable that this unfortunate sequence of events occurred in the following case.

CASE-RECORD

A girl, aged 6 weeks. First child, normal pregnancy, full term. Birth weight 6 lb. 7 oz.; weight on the 7th day 6 lb. 10 oz. Breast-fed until the 17th day, when diarrhœa started, there being twelve loose green stools that day, with slight vomiting. The baby was taken to another hospital, where it was noted that she was severely wasted and that the liver and spleen were palpable. At that time the total leucocytes numbered 7200 per c.mm. (stab forms 3%, neutrophil

Digitized by Google

polymorphs 39%, eosinophils 2%, lymphocytes 53%, monocytes 3%). The mother's Wassermann reaction was negative. Glucose water by mouth was advised, and the diarrhœa and vomiting ceased. However, by this time the mother's breast-milk had failed, so bottle-feeding was started.

A right otorrhœa developed 18 days later, and in a further 2 days the vomiting recommenced; on the following day everything by mouth was returned and there was mucus in the vomits. When taken to hospital the next day only boiled water by mouth for 24 hours was prescribed. The vomiting ceased before the 24 hours were up, so the mother again started milk feeds; and there was further vomiting. For the ensuing 2 days glucose water only was given by mouth, and the child was then sent to this hospital.

On admission, she was moderately dehydrated, with scurf on the scalp and red buttocks. The eyes, mouth, throat and ears, chest, and abdomen showed no abnormality.

Urine.—No pus cells, red blood-cells, or casts seen in the centrifuged deposit. There was a light cloud of albumin.

Blood.—Wassermann and Kahn reactions negative.

Stools.—*Proteus vulgaris* present. Repeatedly negative for *Staphylococcus aureus* and organisms of the salmonella and Shigella groups.

Treatment and Progress.—On admission half-strength Hartmann's solution with 5% glucose was given by mouth, and during the first 18 hours there was no vomiting and no stools were passed. At 10 A.M. next morning one-eighth strength 'Ostermilk No. 1' was started, and in the next 24 hours there were three vomits and five small stools. At the end of that time two very large offensive stools were passed, and the feeds were changed to 'Nestlé's Sweetened Condensed Milk,' one-sixth strength, 2½ oz. 3-hourly. At this time also the right eye was discharging, and penicillin 50,000 units intramuscularly b.d. was started. Cultures from the eye grew *Staph. aureus*.

On the 3rd day after admission fourteen stools were passed, and there were two vomits. At 4.30 P.M. the stomach was washed out and 3 oz. of subcutaneous saline was given. The parenteral fluid was repeated at 12 midnight and at 9 o'clock next morning. Streptomycin by mouth was also started, the dose and method used being that described by James and Kramer (1948). By 3.30 A.M. on the 4th day the *P. vulgaris* had been eliminated, and by 6.30 A.M. the stools were sterile on aerobic culture and remained so for 24 hours. After that time *Streptococcus fœcalis* and coliform organisms reappeared, but only in small numbers.

Progress during the next 2 days was satisfactory, the baby gaining 8 oz.

At 10.15 A.M. on the 7th day after admission there was a sudden collapse. The baby was very pale, cold, and drowsy; her respirations were extremely shallow, her pulse was imperceptible, and her heart sounds could be heard only with difficulty. Despite injection of nikethamide, administration of oxygen, and later artificial respiration, the baby died at 10.45 A.M.

Necropsy.—No cause of the sudden death could be found, the only macroscopical changes being moderate fatty degeneration of the liver and well-marked congestion of the lower part of the small gut. No ulceration was seen. Cultures taken from the terminal ileum gave a very heavy pure growth of a coagulase-positive streptomycin-resistant *Staph. aureus* (heavy growth in streptomycin 1000 units per ml.). Unfortunately by this time the cultures from the eye had been destroyed, so the *Staph. aureus* from that source could not be tested for streptomycin sensitivity.

From the time that streptomycin was started by mouth, every stool passed was cultured on blood-agar, and at no time was *Staph. aureus* isolated. It is evident, therefore, that the organism in the gut had multiplied very rapidly.

The ability of *Staph. aureus* toxin on ingestion to produce acute food-poisoning is widely recognised, but it is less well known that in children the organism is capable of causing enteritis by multiplication in the gut. Felsen and Wolarsky (1942) and Draper and Brown (1946) describe several cases, three of those in the latter's series proving fatal.

It has also been shown (see Waksman 1947) that many of the normal organisms of the alimentary tract are capable of exerting antagonistic effects against staphylococci in vitro, and it is possible that the great reduction or temporary elimination of coliforms which follows the administration of streptomycin by mouth (Smith and Robinson 1945, James and Kramer 1948) may predispose towards such intestinal infection.

SUMMARY

A fatal case of enteritis in an infant receiving streptomycin by mouth is described.

A streptomycin-resistant coagulase-positive *Staph. aureus* was obtained in pure culture from the terminal ileum at necropsy.

It is suggested that the *Staph. aureus*, already present elsewhere in the body, was rendered streptomycin-resistant by the small amount of the drug absorbed from the gut, and that elimination of the normal intestinal flora may have contributed to the establishment of the staphylococcus there.

I am indebted to Dr. Ursula Shelley for permission to use the clinical notes of this case, to Dr. W. H. Hughes who performed the necropsy, and to Sir Alexander Fleming, F.R.S., for his advice and criticism.

REFERENCES

Draper, F., Brown, G. W. (1946) *Med. J. Aust.* i, 469.
Elias, W. F., Durso, J. (1945) *Science*, **101**, 589.
Felsen, J., Wolarsky, W. (1942) *Arch. Ped.* **59**, 589.
James, U., Kramer, I. R. H. (1948) *Lancet*, Oct. 9, p. 555.
Smith, D. G., Robinson, H. J. (1945) *J. Bact.* **50**, 613.
Waksman, S. A. (1947) Microbial Antagonisms and Antibiotic Substances. New York.

TREATMENT OF LOCAL INFECTION WITH DIAMIDINES

F. KOHN
M.D. Prague.
SURGEON, ST. MARTIN'S HOSPITAL, BATH

CLARA D. CROSS
M.D. Sheff., M.R.C.P.
AREA PATHOLOGIST

DESPITE the successes obtained in the past eleven years in treating bacterial infections, some still remain unamenable to treatment. In a high proportion of these, gram-negative rods can be identified either alone or with other pathogens. We have tried to develop a technique for their elimination, mainly confining our attention to surface infections as before (Kohn et al. 1943).

The antibacterial properties of derivatives of the diamidines (Ashley et al. 1942) suggested that they were worthy of clinical trial.

Our first experiments were made with 2 : 2′-dibromo-4 : 4′-diamidino-α-γ-diphenoxypropane or 'Dibrompropamidine' and 2-iodo-4 : 4′-diamidino-α-ε-diphenoxyhexane or 'Iodohexamidine,' which in the absence of convenient short names will be referred to by their laboratory numbers M. & B. 1270 and M. & B. 1314. Owing to limitations in the supply of M. & B. 1314 most of our work was done with M. & B. 1270, but there seems little to choose between the two compounds as regards their action on staphylococci, except that when a strain in a wound has been found insensitive to one it has been sensitive to the other.

Bacteriological studies were made on each case together with appropriate sensitivity tests. Cultures were taken every day or at the time of each dressing, even when dressings were done more than once daily. The routine was to sow a loopful of discharge from the wound on a warmed blood-agar plate directly at the bedside. Blood-agar was used as a routine unless there was any indication for a special medium. In recording the results an arbitrary system of plus signs was used: ++++ indicated a plate completely overgrown, and + the presence of only three or four colonies, ++ and +++ being gradations between these. To prevent contamination of the culture-media with the drug, wounds treated

Digitized by Google

BACTERIA IDENTIFIED

Lesions	No. of cases	*Ps. pyocyanea*	*Proteus vulgaris*	*Bact. coli*	*Staph. aureus*	*Hæmolytic streptococcus*
Varicose ulcers..	12	5	2	1	8	1
Traumatic ulcers	7	3	1	0	4	1
Burns	1	1	0	0	0	0
Open fractures ..	3	1	1	1	3	0
Appendicitis ..	7	0	0	3	0	2
Miscellaneous ..	2	4	0	0	1	2

with semi-solid vehicles were always carefully cleaned with saline before swabbing. Though too much saline on a surface wound might conceivably lead to a negative culture, the results obtained in the large number of cases treated suggest that this fear is unjustified. To satisfy the various opinions held regarding virulence tests on staphylococci note was made of colour changes, extent of hæmolysis, and production of coagulase. Direct films were not considered to be so useful as cultures in the treated wounds, because often bacteria seen in smears did not grow after effective local treatment had begun.

The accompanying table shows that the predominating bacteria were staphylococci and *Ps. pyocyanea*, *Proteus vulgaris* having been identified in only 3 of 32 cases, in contrast to experience in other hospitals. Diphtheroids have been isolated often, but we doubt whether these have much pathological significance in view of the clinical course of our cases once the major infection had been successfully treated. We include 3 cases of *Bact. coli* infection which occurred among 6 cases of mixed sepsis following recently treated appendicitis. Differential bacteriological studies have confirmed the findings of other workers that coccal infections are often overshadowed by *Ps. pyocyanea* in surface wounds, even after supposedly adequate treatment with sulphonamide or with penicillin (see fig. 1).

TREATMENT AND RESULTS

Initially the conditions selected for treatment were various surface lesions, including traumatic and varicose ulcers, open fractures with skin loss, indolent wounds, and an unhealed burn.

In any local treatment of wounds it is necessary to ensure that purely mechanical factors do not prevent access of antibacterial agents to infected tissues. Pockets and sinuses may cause difficulties and if possible must be dealt with on first principles. Should the anatomy of the part restrict wound toilet, topical chemotherapy can be attempted, but the effect is not so dramatic as in more favourable cases.

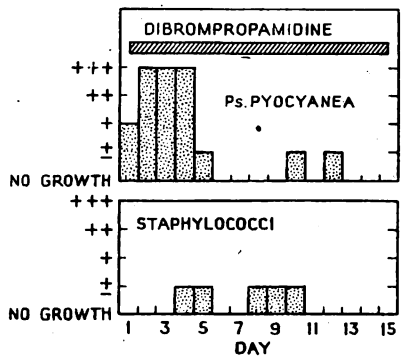


Fig. 1—Bacteriological data in a case of gunshot wound of thigh, showing prevalence of *Ps. pyocyanea*, and effect of dibrompropamidine.

At first we chose long-standing heavily infected varicose ulcers for investigating *in vivo* the action of the diamidines. Such cases are most convenient for assessing antibacterial techniques, especially against gram-negative rods, the principal pyogens outside the range of chemotherapeutic agents at present in general use. With the experience gained from these cases others likely to be more difficult were treated.

There are three obvious ways in which an antibacterial compound can be used for topical applications: in aqueous solution, in a semi-solid vehicle, and as powder. Initially, therefore, on obstinate cases we tested the effect of aqueous solutions. The use of wet dressings for wounds is for technical reasons generally recognised as unsatisfactory; so more attention was paid to the possibilities of semi-solid vehicles and later to the use of powder. We believe that a 1:1000 solution of M. & B. 1270 may, in special circumstances, provide a useful adjuvant to surgery, but to find the optimal concentration for routine use requires further study.

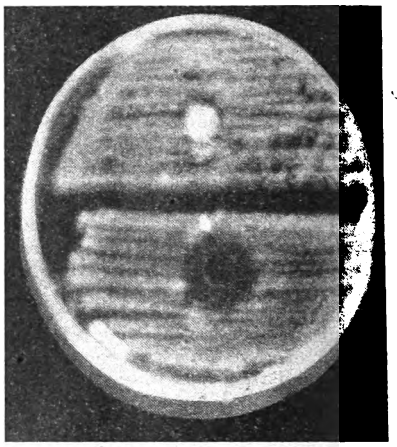


Fig. 2—Inhibition of *Ps. pyocyanea* by dibrompropamidine when pure (below), but not when in a cream (above).

We have examined several semi-solid vehicles generally popular for the local exhibition of antibacterial substances. Initially we used the Mumford base in which was incorporated 0·15% of M. & B. 1270 isethionate—i.e., 0·1% of active product—but this and higher concentrations failed to eliminate gram-negative infections, because of the inhibitory action of the 'Lanette wax.' Use was also made of the base devised by Todd (see Clark et al. 1943), but it was abandoned for the same reason (see fig. 2).

The anticoccal action of M. & B 1270 and M. & B 1314 is exerted in the presence of lanette wax probably because of the high activity of these compounds against gram-positive cocci compared with gram-negative rods. Alternative vehicles have been examined. One consisting of carbowaxes, propylene glycol, and water containing 1–5% M. & B. 1270 shows the greatest promise, and further studies with it are in progress.

Dusting into wounds probably provides the best test of efficiency of any compounds being examined, and this is what we increasingly favour.

We have treated 12 cases of varicose ulcer, 7 traumatic ulcers, 1 burn, 3 open fractures, 2 miscellaneous cases, and 7 cases of acute gangrenous appendicitis, but unfortunately in only 3 of the last was a precise bacteriological examination possible. Some of these cases before coming under our care had received different treatments or no treatment of any consequence. Of 16 cases with staphylococcal infection 6 had had penicillin either alone or combined with sulphonamide therapy.

The local infections fell into two groups; those due to persistence of staphylococci despite intensive treatment with synthetic compounds or antibiotics, and those caused by gram-negative rods. Laboratory tests so often showed that the persistent staphylococcal infections were insensitive or only slightly sensitive to penicillin that routine testing was abandoned. One case from which a penicillin-fast strain of staphylococcus was recovered made slow progress when treated with M. & B. 1270 despite demonstrable sensitivity to it in vitro. Change to M. & B. 1314 eliminated the infection in five days, and spontaneous healing took place four days later (fig. 3).

We treated 10 cases of gram-negative infection with one or more bacteria in various ways before a successful

Digitized by Google

technique was evolved. Among the early cases were some treated unsuccessfully with penicillic acid both in aqueous solution and in powder, application of the latter being painful. M. & B. 1270 and M. & B. 1314 were applied in various ways with significant but not convincing results until used in powder form or incorporated in amounts up to 5% in the new carbowax base previously mentioned. In 14 successive cases of gram-negative and coccal infection the infections were eliminated in not more than seventy-two hours. The wounds if small were allowed to epithelialise spontaneously beneath the serum scab which formed after successful local treatment, or they were grafted in the usual manner. The over-all clinical results of the new treatment can best be shown by the short stay in this hospital of patients with persistent sepsis. Owing to the lack of adequate data for a truly comparable control series this shortening of hospital stay cannot be expressed statistically, but the change which has now taken place is apparent to everyone.

In our early successful cases the appearance of a serum scab over large wounds, which rarely if ever became covered thus, raised the question whether the scab might have been the result of some local toxic or sclerosing effect of M. & B. 1270. This seemed unlikely in view of the close adherence of the scab to underlying granulations. For this reason biopsies were done and serial sections were made of tissues removed in the ordinary way at the time of grafting three days after the start of treatment. A typical specimen is shown in fig. 4, in which the edge of the serum scab can be seen with

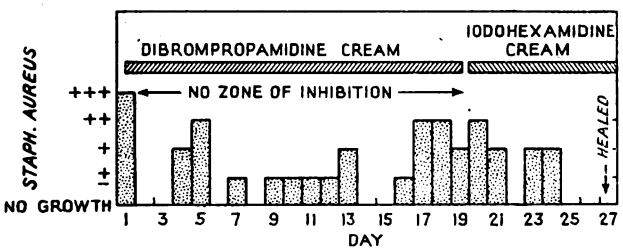


Fig. 3—Bacteriological data in a case of traumatic ulcer of leg, showing effect of changing treatment from dibrompropamidine cream to iodohexamidine cream.

squamous epithelium passing beneath it. The serum scab is adherent to normal young granulations and new vascular loops, and there is a complete absence of any pyknosis or polymorphonuclear reaction.

As a further test of local reactions another case was taken. This was a long-standing varicose ulcer heavily infected with *Ps. pyocyanea* and in which two unsuccessful attempts at grafting had previously been made. The middle third of the wound was treated with M. & B. 1270

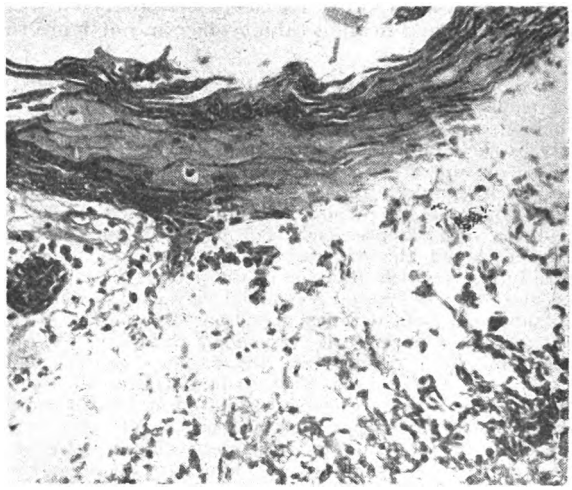


Fig. 4—Section of wound edge showing squamous epithelium extending under serum scab after treatment with dibrompropamidine. (× 225.)

powder, the remainder being covered with soft-paraffin gauze. Fig. 5 shows biopsy specimens from the control and treated areas respectively. In the control the characteristic changes of an infected ulcer are visible, whereas the treated area shows a serum scab adherent to underlying new granulations devoid of any inflammation. Sections from other cases confirm these findings.

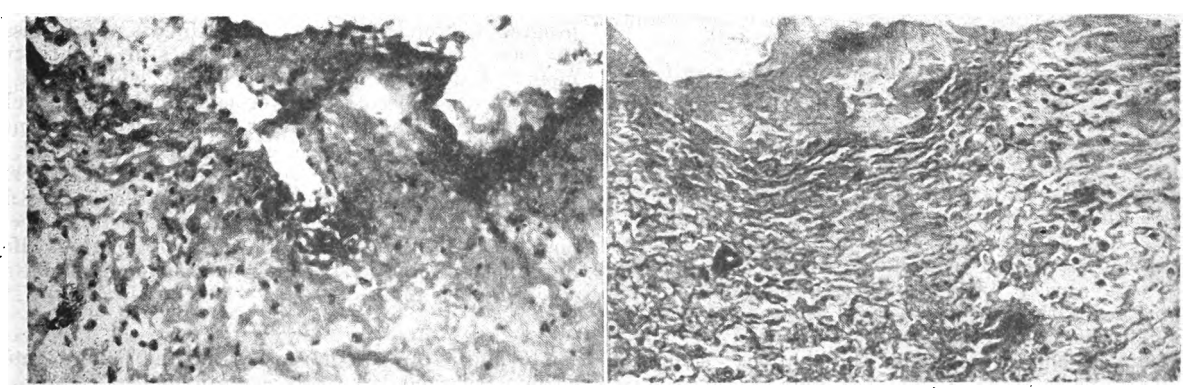
The time that treatment should be continued is determined not only by the bacteriological findings but also by the type of wound and its pathology. With soft-tissue wounds results are quicker, and the time of treatment is shorter, than in lesions with much trophic disturbance, such as leg ulcers or those following neural lesions. In most cases significant infections can be eliminated in 72 hours and a decision made about further procedures such as grafting, secondary suture, or even natural healing.

We have found no evidence of general toxicity after the local application of M. & B. 1270 or M. & B. 1314, even when the former is placed in the peritoneal cavity.

ILLUSTRATIVE CASES

Intra-abdominal Sepsis

We have treated 7 cases of appendix abscesses, of which 3 were due to *Bact. coli* and hæmolytic streptococci, and 1 case of generalised peritonitis. This was done by placing 0·5 g. of M. & B. 1270 in the abscess cavity at the operation, one being a particularly severe case with an acutely inflamed friable cæcum. Tube drainage was provided in all cases at the time of operation, but dis-



a *b*

Fig. 5—Varicose ulcer: *a*, untreated area; *b*, area treated with dibrompropamidine. (× 225.)

Digitized by Google

charge ceased so rapidly that tubes were removed within 48–72 hours, final healing taking place in not more than 14 days.

Case 1.—The case of general peritonitis secondary to gangrenous appendicitis was particularly instructive, because it demonstrated not only the action that M. & B. 1270 can exert in such infections but also its freedom from irritant effects. At operation a gangrenous appendix was found in pus which spread all over the abdomen. This pus was mopped out as far as possible, and films of it showed coliform organisms and streptococci; 0·5 g. of M. & B. 1270 was sprinkled round the cæcum, and the parietal wound was partially closed, with drainage of the pelvis. The patient, a man aged 19, was treated postoperatively with penicillin and sulphonamides, and detailed attention was paid to his fluid balance, but he never really responded and he died ten days after admission. At necropsy the findings were typical of such a case, except that in and round the cæcal area the visceral peritoneum was glistening and normal in all respects, without any fibrinous exudate or adhesions. In other words, were it possible to provide for a more widespread effect of M. & B. 1270 in the general peritoneal cavity, the life of such a patient might be saved.

Fractures

Case 2.—A man, aged 30, with an ununited open fracture of the tibia and fibula and considerable loss of overlying skin, was considered to need bone grafting. There was a scar measuring 18 sq. cm., covered with unhealthy granulations containing pathogenic *Staph. aureus*.

Powdered M. & B. 1270 was applied for 48 hours, at the end of which time culture was negative. A pedicle graft from the other leg was applied in two stages, and complete healing took place by first intention. The donor site was open and became infected with the same bacteria. Application of M. & B. 1270 for 48 hours cleaned this area, a Thiersch graft was applied, and the wound completely healed in a week.

Case 3.—A man, aged 26, had sustained an open fracture of the right tibia close to the ankle three and a half years earlier. Immediately after the accident he had been admitted to hospital, where he had remained for twelve months, undergoing first-class surgical treatment, with adjuvant penicillin and sulphonamides for the sepsis which developed. The sepsis had persisted, and further local and general penicillin therapy had been given without effect. Bony union had ultimately taken place, but he had been left with a large bone and skin defect measuring 4 cm. across and 2·5 cm. deep. In various hospitals attempts had been made without success to control the local sepsis and effect a repair. When we saw him he had the discharging wound just described, from which a pathogenic staphylococcus was isolated. M. & B. 1270 powder was dusted into the wound for 2 days. A sterile serum scab formed. This was removed, a Stent graft was applied, and the wound healed in a fortnight from the time of admission.

Varicose Ulcer

Case 4.—A man, aged 71, had had a varicose ulcer for many years. It measured 71 sq. cm. and was covered by typical necrotic material. *Ps. pyocyanea* was obtained in pure culture. M. & B. 1270 powder was applied twice daily for two days and then daily for two more days, at the end of which the wound became sterile and was immediately successfully grafted.

Reinfection.—In the early cases treated it was found that, if grafting was delayed, the wound might soon become reinfected with gram-negative bacilli. Cultures made from the skin edges just beyond a wound rendered sterile by M. & B. 1270 powder yielded a growth of similar gram-negative bacilli, and it seems that from these edges a wound may become reinfected unless countermeasures are taken. The procedure adopted initially was to dust the wound twice daily, well beyond the skin edges, with a very finely ground powder applied with a pepper-pot with many small holes, the area afterwards being covered with plain gauze. We used the small screw-capped bottles in which the "bijou" slopes of medium are contained, removed the rubber disc, and made small holes in the screw top. A sulphanilamide insufflator might be used for dusting.

DISCUSSION

Many patients had received various local applications before M. & B. 1270, in powder and more recently in carbowax base, was applied with good effect, but the previous long treatment might have rendered the infecting strain more sensitive to the new agent. Two fresh cases of varicose ulcer, both of six months' duration, were therefore selected. Neither case had had any specific treatment and both were infected only with *Ps. pyocyanea*. Clinically the effects were equally striking, because discharge ceased and the raw surface became covered with a serum scab firmly adherent to underlying healthy granulations. To save the time necessary for spontaneous healing these wounds were successfully grafted forthwith despite the fact that natural healing seemed likely to take place.

The results of treating ordinary surface wounds with M. & B. 1270 in semi-solid vehicles justify its use as a local application for the routine treatment of superficial infections. No special storage precautions are necessary. The range of activity appears to be governed by the vehicle used. For infections in which gram-negative rods predominate a carbowax base will be necessary, but M. & B. 1270 in Todd's cream is effective in coccal infections, besides relieving the pain in some staphylococcal infections, a property which does not seem due simply to the bland nature of the base. Two cases of persistent painful staphylococcal ulcers had had, without effect, various applications including cream bases exactly similar to that used to exhibit the new compounds. Within a matter of hours relief was obtained and continued, the most likely explanation being that proliferation of virulent staphylococci was checked; recovery was rapid.

It is contrary to generally accepted ideas about the inhibition of bacterial activity that a single compound can provide an effective local treatment of surface infection by such morphologically different bacteria as those under review. However, Bernheim (1944) has shown that a simpler diamidine, 'Propamidine,' inhibits the oxidative metabolism of certain gram-negative bacilli.

In all our treatments the results do not seem to have depended on the quantity of compound used so much as on how it was used. We have not finally decided whether better results accrue from the application of pure powder than from admixture with a suitable diluent. It is likely that the indications for and methods of using M. & B. 1270, and M. & B. 1314 in powder form will make skilled supervision necessary to obtain the best results and avoid a foreign-body reaction, but the use of existing cream preparations is only limited by their range of antibacterial action. It is also likely that cream preparations can in some circumstances be beneficially used after initial treatments with powder.

Touching the methods available for recording the progress of wounds, the rate of healing is not necessarily the best way of recording the effects of aids to treatment. Many infected wounds for a while make fair progress which becomes slower as fibrous tissue develops. The early application of grafts, and the use of secondary suture whenever possible, introduce an artificial, but highly desirable, complication to studies of healing rates. Bacteriological studies on wounds undergoing treatment may, if taken at their face value, be misleading because positive cultures can be obtained despite obvious clinical improvement as soon as antibacterial compounds start to exert their effects.

SUMMARY

The effects of dibrompropamidine and iodohexamidine on infected wounds have been examined.

Dibrompropamidine powdered into surface wounds inhibits infections with gram-negative bacilli, *Ps. pyo-*

Digitized by Google

cyanea, and *Bact. coli*, and it may find a place in the treatment of appendix abscess and resultant peritonitis.

Dibrompropamidine in castor-oil cream provides a convenient non-toxic practical alternative to sulphonamides and penicillin for the treatment of surface infections with gram-positive cocci. In a carbowax propylene-glycol base its action on gram-negative organisms is also manifest.

From the limited experiments made with iodohexamidine it seems to provide a useful alternative to dibrompropamidine when bacterial strains initially resistant to the latter are encountered.

We have drawn on the knowledge and experience of Dr. W. R. Thrower in the field of chemotherapy, and we are grateful to him for this and for his vision regarding many problems still outstanding.

Our thanks are due to Miss Daphne Miller and Mr. J. B. Staniforth for much technical assistance, to Messrs. May & Baker Ltd. for supplies of the compounds used, and to Messrs. Gillette Industries Ltd. for the photomicrographs.

REFERENCES

Ashley, J. N., Barber, H. J., Ewins, A. J., Newbery, G., Self, A. D. M. (1942) *J. chem. Soc.* p. 103.
Bernheim, F. (1944) *J. Pharmacol.* 80, 199.
Clark, A. M., Colebrook, L., Gibson, T., Thomson, M. L., Foster, A. (1943) *Lancet*, i, 605.
Kohn, F., Hall, M. H., Cross, C. D. (1943) *Lancet*, i, 140.

ALGINATES IN ENDAURAL WOUND DRESSING

E. R. GARNETT PASSE
V.R.D., F.R.C.S., F.A.C.S., D.L.O.
CONSULTANT AURAL SURGEON, KING EDWARD MEMORIAL HOSPITAL, EALING

GEORGE BLAINE *
L.R.C.P.E.
STRANGEWAYS RESEARCH LABORATORY, CAMBRIDGE

THE success of endaural operations, especially the fenestration operation, largely depends on a suitable postoperative dressing. Unless one obtains a dry cavity which heals by first intention in a minimum of time, epithelisation is complicated by excessive granulations, especially over bared bone.

Until recently one of us (E. R. G. P.) has used an absorbable cellulose packing which, as it liquefies, can be sucked out of the cavity on the tenth day. This has already proved an advantage over other materials with which it is necessary as a routine to perform four or more dressings, the first always under anæsthesia (Passe 1947).

Tumarkin (1948) has also emphasised the importance of postoperative dressings in transmeatal attico-antrotomy, recommending the use of a gel formed from a mixture of penicillin and 'Zelex,' which is mainly composed of an alginate base.

In a search for an ideal endaural dressing, alginate materials were submitted to extensive trials during the last six months. Based on the work of one of us since 1944 (Blaine 1946, 1947a and b), a wide range of materials has now been made available with properties which might make them eminently useful for this purpose.

Alginate is an extract of the brown seaweeds growing off the Scottish and Irish shores, the parent substance being alginic acid, a polyuronic acid whose sodium salt combines with calcium ions to produce an insoluble gel. This reaction makes it possible to produce fabrics like wool, gauze, and foam; it has been found non-antigenic, sterilisable by heat, hæmostatic, and slowly absorbable in living tissue according to the vascularity of the tissue into which it is placed. Alginate is rendered soluble by solutions of sodium salts. The introduction of a variable percentage of sodium ions into calcium-alginate fabrics makes possible the production of a range of materials of variable solution-rate and absorption-rate. Antibacterial substances can be combined with these in the course of production.

Advantages of Alginate Dressing.—One of us (G. B.) has found in experimental surgical studies that calcium alginate is usually slowly absorbable in living tissue without inducing excessive formation of fibrous tissue. It is hæmostatic and a poor culture medium for micro-organisms. Alginate materials in which the percentage of sodium ions is raised by industrial chemical treatment over that of calcium ions are absorbed with far greater rapidity and with a minimal reaction. The speed of absorption or of solution again depends on the vascularity of the tissue into which it is placed. Thus, as an endaural wound dressing, where meticulous hæmostasis has been achieved and where there is only a little serous oozing, the alginate gauze or wool displays the following properties:

(1) Where the dressing is in contact with the oozing surface it is converted into a smooth jelly.

(2) Parts of the dressing not in contact with a moist surface remain, on the whole, unaltered.

(3) It can be easily packed into crevices, conforming closely to the contour of the surface to which it is applied. Dipped into saline solution, Ringer's solution, or water (according to the grade of material used) immediately before use, it becomes a truly plastic dressing which securely keeps skin flaps in place.

(4) The alginate dressing can be left in situ for the whole period of convalescence without being changed.

(5) Removal is effected by gentle withdrawal or by dissolving the material in the solvent at the grade used (saline solution, sodium citrate, or water). In the case of the water-soluble alginate grades a good part of the dressing will liquefy by the time it is to be removed.

Composition.—In these trials the following grades of alginate ribbon gauze and wool have been used:

(*a*) Calcium alginate containing cetyl pyridinium bromide (C.P.B.), an antibacterial agent akin to cetrimide ('Cetavlon.')
(*b*) 80% sodium-calcium alginate containing C.P.B.
(*c*) 20% sodium-calcium alginate containing C.P.B.
(*d*) 20% sodium-calcium alginate with 5% borax, containing C.P.B.

CONCLUSIONS

Alginate dressing is by far the most satisfactory for the aural surgeon. It can be left in situ for three or four weeks; it prevents excessive formation of granulation tissue; it obviates the patient's anticipation, fear, and discomfort of repeated dressings; and it reduces the work of the aural surgeon. Sulphadiazine and/or 'Phenoxetol' can be added to alginate dressings, though the material is a deterrent to bacterial growth owing to its content of cetyl pyridinium bromide. On removal of the dressing the cavities always appear smoothly healed and clean with the healthy pale-pink skin flap held firmly in place over the fenestra.

When used after radical endaural mastoidectomy the alginate dressings proved themselves equally excellent. In these cases the dressing was applied after preliminary sprinkling of the wound with sulphadiazine and penicillin powder. The dressing was usually changed after seven to ten days, when the healing cavity was repacked with a fresh alginate dressing. Both the wool and gauze were found to be satisfactory.

The Scottish Research Association, Messrs. Courtaulds Ltd., and Optrex Ltd. provided chemical information and materials for this trial.

REFERENCES

Blaine, G. (1946) *Lancet*, ii, 525.
— (1947a) *Ann. Surg.* 125, 102.
— (1947b) *Med. Pr.* 218, 166.
Passe, E. R. G. (1947) *Post-grad. med. J.* 23, 507.
Tumarkin, A. (1948) *Proc. R. Soc. Med.* 40, 761.

* Working with a Leverhulme research grant of the Royal College of Surgeons of England.

Digitized by Google

Reviews of Books

The Mechanism of Abdominal Pain

V. J. KINSELLA, CH.M., F.R.C.S., F.R.A.C.S., surgeon, St. Vincent's Hospital, Sydney. Sydney: Australasian Medical Publishing Co. 1948. Pp. 230. 32*s.* 6*d.*

IN this book Mr. Kinsella attempts to connect abdominal pain with particular nerve paths and to explain the phenomena of abdominal sensation anatomically. He begins with a historical outline of past research, which makes it clear how difficult the subject is. His main thesis is that pain nerves in the viscera are of splanchnic origin and do not differ essentially from sensory nerves elsewhere. Clinical experiments are cited which seem to show that inflamed organs are sensitive to pressure; but the explanation of why it is possible painlessly to cauterise and cut intestine or stomach withdrawn from the peritoneal cavity is not very convincing. The existence of an "irritable focus" substance acting in the central nervous system is postulated, but no evidence for it is brought forward except the argument of analogy. Clinically the author is undoubtedly right when he insists that deep tenderness is the best guide to the inflamed viscus. The later chapters, in which the pains of different diseases are explained in the light of the author's hypotheses, are very interesting.

The emotional make-up of different people is so different that their responses to pain are scarcely comparable; and the difficulty in arriving at truth in studies based on subjective expressions is extreme. This book, if it does not much advance the knowledge of visceral pain mechanism, is stimulating; and Mr. Kinsella's critical attitude to previous work will be a great help to anybody entering this field of investigation.

Present Status of the Surgical Treatment of Hyperthyroidism

WARREN H. COLE, M.D., professor and head of the department of surgery, University of Illinois; EDSON FOWLER, M.D., assistant in surgery in the department. Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1948. Pp. 81. 10*s.* 6*d.*

THIS brief monograph comes from the department of surgery in the University of Illinois, Chicago. Though it does not attempt to cover the whole field of thyroid surgery, it effectively displays the more important features. The authors' aim has been to emphasise subjects of moment at the present time, and this they do without waste of words. The position of the antithyroid drugs is fairly and clearly summarised; though (unless the patients are carefully selected) it seems over-optimistic to suggest that more than half of those treated with propyl thiouracil will experience lasting remissions. The little said about the use of radioactive iodine in toxic goitre is not in its favour. Preoperative treatment is well described, as well as the criteria by which safety for operation is determined. The operative technique seems to differ little from that practised in Great Britain, and indeed the whole subject seems to have reached very much the same position in the United States as here.

Jaundice

Its Pathogenesis and Differential Diagnosis. ELI RODIN MOVITT, M.D., acting chief of medicine, Veterans Administration Hospital, Oakland, California. New York and London: Oxford University Press. 1947. Pp. 261. 42*s.*

A BOOK devoted to jaundice is particularly welcome at the moment because of the current widespread interest in disease of the liver, the recent extensive epidemics of infective hepatitis, and the importance of accurate diagnosis before treatment. The first part of this work, devoted to anatomy, physiology, and diagnostic procedures, is reliable and critical. Unfortunately though there are some 180 references at the ends of the chapters, the text mentions hardly any of them, and the reader is therefore left with no ready means of verifying such surprising statements as that "a number of individuals diagnosed as diabetes, and being treated as such, actually suffer from liver insufficiency rather than the insufficiency of insulin," or that "the liver serves as the largest depot of vitamin C." Despite this, part I is a comprehensive and useful contribution to the literature on tests of liver function. Part II, which gives a textbook description of the three main types of jaundice—hæmolytic, parenchymatous, and obstructive—does not maintain the same standard. The section devoted to toxic hepatitis is weak, and the relation of nutrition to liver disease is almost entirely relegated to a misleading footnote in which the terms toxipathic and trophopathic are incorrectly used, again without reference to original papers. A startling omission is the absence, in a long discussion of arsphenamine jaundice, of any reference to syringe-transmitted hepatitis. Nevertheless the book as a whole contains information of great value to all responsible for the care of jaundiced patients.

Introduction to Diseases of the Chest

(3rd ed.) JAMES MAXWELL, M.D. Lond., F.R.C.P., physician, to the Royal Chest Hospital, and to the Ministry's Mass X-ray Unit. London: Hodder & Stoughton. 1948. Pp. 308. 12*s.* 6*d.*

IT is seldom difficult to find technical faults in a textbook for students: presentation of a subject simply, logically, and without argument, inevitably involves some over-simplification. This book is not without such faults, but it is nevertheless a very good book, omitting little that is important. The present edition differs from the second chiefly in including radiography as part of physical examination of the chest rather than as the first of the special investigations—an enhancement of status designed to impress its importance on the student.

The opening chapters, dealing with history-taking and physical examination, are particularly helpful, and it is comforting to find so experienced and dogmatic an author hedging a little over the exact significance of bronchovesicular breathing. The ætiological classifications of such conditions as lung abscess and pleural effusion are precisely what the student needs; that concerning carcinoma of the bronchus is a fraction too sketchy. The illustrations, gathered together at the end in the form of an atlas, make a moderately good representative collection.

First-Year Physiological Technique (London: Staples Press. 1948. Pp. 84. 7*s.* 6*d.*).—This excellent booklet is written in so light a vein that it is tempting to make a laudatory pun on Dr. Alex Comfort's surname. There is a full pennyworth on every page and no student should be without it.

Essays on Historical Medicine (New York: Froben Press. 1948. Pp. 220. $5.).—Dr. Bernard J. Ficarra's book is a series of essays on more or less related subjects—a potpourri of persons and events in medical history. In general, the outlook is surgical, and he gives pride of place to the rapid progress of American surgery, more particularly abdominal surgery—progress dramatic in scope as well as in speed. Among the more general essays the references to surgery in Shakespeare claim attention, as do the details of famous men and women who have suffered from some physical disability and yet overcame this and lived to benefit their fellow men.

British Juvenile Courts (London: Longmans, Green for the British Council. 1948. Pp. 44. 2*s.*).—Mr. John A. F. Watson begins his short book by citing the cases of a boy of 13 hanged at Maidstone in 1831 for theft, and of another of 9, sentenced in 1833, but not executed, for breaking a window. From this starting-point he describes the circumstances and procedure of the modern English juvenile court, and the disposal of offenders. The text is readable and accurate, and though it tends in places, especially in its choice of illustrations, to become an apologia for the system it describes, it will prove useful as a source of facts both in England and (as its publication for the British Council foreshadows) abroad. The author is himself a court chairman, and the reasonableness and humanity of his attitude might well be an object lesson to those who deal with adult offenders, where the contrast with 19th century penology is less evident. The Lord Chancellor, Viscount Jowitt, contributes a judicious preface.

Digitized by Google

'everything seems to go wrong . . .'

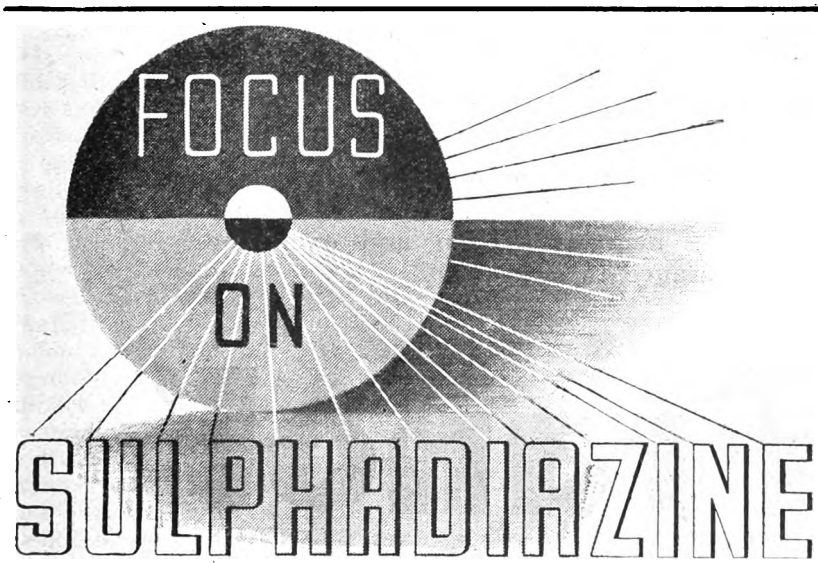
How often you hear it in your surgery! People today, harassed and run down, find themselves unable to contend with all the small irritations and minor mishaps of life.

Livogen is invaluable in all cases of nervous depression, reduced vitality and general debility. It restores vitality rationally, by supplementing the normal resources of the body. It is a balanced composition of liquid extract of liver B.P., extract of yeast, vitamin B_1 and nicotinic acid. Bottles of 4 and 16 fluid ounces are available as well as bottles of 80 fluid ounces for dispensing. Literature is available to medical men on request.

LIVOGEN
Trade Mark

MEDICAL DEPARTMENT
THE BRITISH DRUG HOUSES LTD. LONDON N.1
TELEPHONE: CLERKENWELL 3000 TELEGRAMS: TETRADOME TELEX LONDON

Lgn/E/95



for EFFECTIVENESS
LOW TOXICITY
BLOOD-LEVEL MAINTENANCE

EVIDENCE accumulated during recent years indicates that Sulphadiazine is probably the most highly esteemed sulphonamide throughout the world.

Its effectiveness against many bacteria; its low toxicity, and the ease with which blood-levels can be maintained following its use, all establish a preference for Sulphadiazine.

The physician will find Sulphadiazine Lederle the dependable sulphonamide in the majority of the commoner bacterial infections.

Sulphadiazine Lederle is available in bottles of 100 and 1000 0.5 Gm. scored tablets.

Lederle Laboratories
DIVISION
CYANAMID PRODUCTS LTD
FITZHAM HOUSE, LANCASTER PLACE, LONDON, W.C.2

Digitized by Google

ASTHMA — aborting the night attack

In a new paper (*Practitioner*, June 1948, p. 468-9) the author attributes to 'Franol' the power of suppressing nocturnal asthmatic attacks in patients who otherwise are awakened regularly in the early hours. Under 'Franol' treatment they gain in weight and appetite and are much better fitted to lead a normal life.

The author states that, of the many preparations tested, 'Franol' gives the best results, through the actions of theophylline (on bronchial musculature), ephedrine (on nerve endings) and 'Luminal' (centrally); there is probably some potentiation since the dose of each component is small.

One tablet at night and one on rising appears to meet most needs, and by-effects are rare: the 'Luminal' in 'Franol' mitigates nervous tension and overcomes any individual intolerance to ephedrine.

'Franol'

TRADE MARK BRAND OF

ANTI-ASTHMATIC

SUPPLIES { *Packings of 20, 100, 500, 1000 tablets. Each tablet contains gr. 0·15 ephedrine, gr. 2 theophylline and gr. 0·125 'Luminal'.*

BAYER PRODUCTS LTD • AFRICA HOUSE • LONDON • W.C.2

Digitized by Google

THE LANCET

LONDON: SATURDAY, OCT. 23, 1948

Prefrontal Leucotomy

"PSYCHIATRISTS have been consistently pessimistic about modern physical methods of treatment of mental illness, and consistently wrong," said Dr. DESMOND CURRAN in his Croonian lectures to the Royal College of Physicians last week. Among such methods, prefrontal leucotomy, first done in Lisbon in 1935, has now a long enough history to justify some assessment of its value. Experience has shown that the plane of the cut is important. If too far back it may cause profound stupor, severe personality changes, or even death; and the most satisfactory plane proves to be just in front of the tip of the anterior horn of the lateral ventricle, in about the line of the coronal suture. Dr. ALFRED MEYER, who, at the London County Council's Central Pathological Laboratory, has examined a number of brains in which the operation has been done, has found great variety in the site of the cut; only 10–15% of the corticothalamic fibres may have been divided, and in one case the surgeon had failed to hit the brain at all. The mortality is low, however, and was given in the Board of Control report on prefrontal leucotomy [1] as 3 per 1000. Convulsions are an occasional sequel, but are usually isolated, and seldom persist beyond eight months after the operation. Dr. CURRAN mentioned two patients with idiopathic epilepsy who had no further fits after prefrontal leucotomy. Other occasional sequels are temporary urinary or rectal incontinence, apathy, and transient disorientation. The blood-pressure falls somewhat, and stays a little lower than before operation, even in hyperpietics. The appetite improves, and there may be a period of gross overeating. The patient commonly looks younger and handsomer, and sexual desire is increased, though it usually returns to normal within about a year. A severe reaction after the operation does not necessarily mean a bad prognosis: on the contrary, it almost seems to carry a good one. Common reactions are apathy, irritability, confusion, euphoria, or restlessness; but these gradually wear off, especially if the patient is given opportunity for reablement. W. FREEMAN and J. W. WATTS relate the response to the previous personality of the patient, and to the plane of the cut—finding that euphoria is associated with a forward cut, and apathy with a cut placed far back. The inertia gradually wears off, however, and often gives place to a shallow, cheerful, prankish mood. The attitude of the patient towards incontinence is objective. "What's the weather like with you?" asked one, passing water while she telephoned. "It's raining here."

Dr. CURRAN noted that American opinion is less optimistic than British opinion about the results of the operation. Americans emphasise the fatigability of these patients, their shallowness, and their lack of perseverance; but in Dr. CURRAN's experience these drawbacks are commonly less after six months, and FREEMAN and WATTS found some of their cases doing better after five years than after two. The patients have less capacity for self-blame, and in their work they favour speed before accuracy. F. L. GOLLA holds that their power of ethical evaluation is impaired. Ultimately, however, the success of the operation turns on how the patient feels, what he can do, and what others make of him. His behaviour and capacity must be compared with these things before operation, and his capacity for social relationships must be discovered by asking his friends about him. If they complain that he is not perfect it is well to remember that people in whom the corticothalamic tract remains undivided are not always easy to live with, and that a satisfactory family is necessary for a good recovery. Jewish patients often respond well because family feeling is strong among the Jews. A relatively imperceptive husband or wife, one not easily perturbed by trifles, is a great standby. Those who report, for instance, that a patient was "aggressive" after leucotomy tell nothing unless they say whether his family minded his aggressiveness. Relatives can often estimate the meaning of a patient's behaviour better than the doctor can; and they may be especially helpful when operation is being contemplated, since they can judge whether the patient is suffering real distress of mind or not. Dr. CURRAN mentioned the case of a complaining patient whom he took to be feeling little genuine distress till a member of her family said: "She's not querulous for the sake of being querulous, but because she is anxious and afraid." Emotional tension is the main indication, and the prognosis is related to its degree—to the "amount of tortured self-concern" the patient suffers. Nevertheless some schizoid patients who show little sign of emotional tension respond well—evidence that despite their outward calm their emotional response to their ideas is still strong. A deteriorated schizophrenic, on the other hand, "looks and acts the same with or without his frontal lobes." The prepsychotic personality has some bearing on the result. Those who had a cruel streak, or sought refuge from responsibility, possibly in alcohol, often do badly. The operation has been used in an attempt to reduce the restlessness of hyperkinetic mental defectives, but without much success; those who improved relapsed quickly. On the whole, the better the intelligence the better the result.

It is noteworthy that in America the operation, though not greatly valued for mental states, has been used considerably in the treatment of intractable pain—for instance, the pain of incurable cancer. Though it does not ease the pain, leucotomy may free the patient from the dread of it, and for some reason

1. Prefrontal Leucotomy in 1000 Cases. London: H.M. Stationery Office. 1947. See *Lancet*, 1947, i, 265, 258.

Digitized by Google

he then finds it altogether more bearable. New versions, including transorbital leucotomy [2] and ablation of part of the frontal lobes, are still on trial.

Advances in Microscopy

IN the last fifteen years three new methods of microscopy have been developed which promise great advances in our knowledge of biological fine structure. The principles of phase-contrast microscopy were demonstrated by ZERNIKE in Holland in 1934; the first practical compound electron microscopes were built by RUSKA and MARTON in the same year; and since 1943 BURCH has constructed the first high-performance reflecting microscope.

With the development of the apochromatic objective in 1878 the lens microscope rapidly attained a performance approaching its theoretical limits. Oil-immersion lenses with numerical apertures approaching 1·5 can resolve objects down to a third of the wavelength of light—for sodium light this would correspond to a particle diameter of 2000 Å, or 0·2 μ. By using ultraviolet light of shorter wavelength the resolving power can be further improved to below 1000 Å; but, since glass is opaque to ultraviolet, quartz-fluorite lenses have to be used. Unfortunately, these lenses are monochromatic, so they can only be used for photomicrography and accurate focusing requires a series of trial-and-error exposures. The limit of this technique is set by the opacity of the objective in the far ultraviolet region. However, many biologically important compounds (e.g., nucleic acid) strongly absorb ultraviolet light of selected wavelengths, and the U.V. microscope has therefore proved valuable for qualitative and quantitative estimations of such materials within the cell. This method has been widely used in studies of malignant cells, and such studies can be made on the living cell.

The phase-contrast microscope is also particularly valuable in the study of living cells, though in resolving power it is no better than the normal lens system. When a completely transparent colourless object is viewed in the ordinary microscope, differences in refractility in parts of the object are visible only at the *boundaries* between the regions of different refractive index. In this way the nucleus, chromosomes, cilia, and flagella are seen bordered by light or dark lines. Under phase-contrast illumination the effect produced is that of staining all refractile objects with a neutral grey tint whose depth is a measure of the refractility of the object. The internal details of many of these refractile bodies can be studied; vacuoles in a flagellum and chromosomes in the nucleus are often clearly seen. Phase-contrast illumination can be adapted to any ordinary microscope, but it requires a special condenser and objective. The condenser has an annular stop, so that a ring of light is brought to a focus at the back of the objective. The "phase-plate" in the objective is a flat glass plate with an annular channel a quarter of a wavelength in depth cut in its surface; the plate is so placed that the image of the condenser annulus falls exactly in the groove, and the groove is darkened to absorb part of this undiffracted light which passes through it. Diffracted light from the object passes through the remainder of the phase-plate; it is the interference of the undiffracted and diffracted beams which produces the intensity differences in the final image. This method of examination is not suitable for thick layers of tissue, thick cells, or cells whose cytoplasm is densely packed with refractile granules. But individual cells in tissue-culture are ideal objects for it; cilia and flagella give clear "solid" images and not fictitious diffraction patterns; the structure of striated muscle-fibres and banded chromosomes is sharply defined; and bacteria, spirochætes, and similar bodies are revealed almost as well as by dark-ground illumination. HUGHES and BARER have shown some of the possibilities of this method in their studies of cell division and the structure of muscle-fibres.

The new reflecting microscope which Mr. C. R. BURCH, PH.D., F.R.S., is working on at Bristol overcomes many of the defects inherent in a lens microscope.[1] The mirror objective is completely achromatic and has a minimum of spherical aberration, with an effective numerical aperture of 0·65, but it has a working distance of nearly 2 cm. These features give it the optical performance of a 4 mm. lens objective with the working distance of a low-power binocular. The advantages of this in studies employing microdissection or involving high temperatures and pressures can readily be appreciated. An oil-immersion component can be added to raise the numerical aperture to 0·98, and future models are projected with the resolving power of a normal 2 mm. oil-immersion lens. These achromatic systems have the enormous advantage of complete interchangeability of visual and ultraviolet illuminating sources, without change of focus. Since the reflecting power of a mirror surface can extend into the far ultraviolet, well beyond the limits of a quartz-fluorite lens, the resolving power of this new microscope promises effective magnifications several times those achieved with the U.V. lens microscope. The reflecting microscope is at present an elaborate and exceedingly costly apparatus. So far its gourd-shaped mirrors have required more than 100 hours of skilled and accurate hand-polishing, but the problem of shaping them mechanically is being energetically studied. The achromatic characteristics of these microscopes are likely to find their most valuable application in absorption spectrophotometry of living and fixed material.

The electron microscope owes its origin to the fact that narrow conical pencils of electrons moving at high velocity can be focused by magnetic or electrostatic fields precisely as light is focused by a lens system. The electrons are emitted by a hot filament and are accelerated along the microscope by a high-voltage source. Very accurate control of the voltage produces a "monochromatic" beam of electrons of constant velocity. Most modern electron microscopes use magnetic lenses, which are short solenoids with accurately ground internal pole-pieces; the focal length of the lens can be altered by varying the current passing through the solenoid, so a large range of magnifications can be achieved with a single lens system. The numerical aperture of the objective

2. Freeman, W. *Lancet*, Sept. 4, p. 371.

1. Nuffield Foundation. Report of the Trustees for the Year Ending 31 March, 1948. Oxford, 1948; p. 21.

Digitized by Google

is only about 0·001, but, since the equivalent electron wavelength is 5×10^{-10} cm., this gives a resolving power of 50 Å—some forty times better than the best results with the optical microscope. Experimental models have been built to resolve 10 Å, which should make visible spherical molecules consisting of about 100 atoms. The possibilities of the instrument for biological research are therefore enormous. That it has not yet realised the dreams which it first inspired is due to difficulties in the preparation and mounting of the specimen, which must be less than 0·1 μ thick and, since the microscope is evacuated to a very low pressure, must also be completely dry. Thick specimens absorb too much of the energy of the beam, and, apart from their consequent opacity, may be destroyed by the heat which is liberated in them. For this reason the most successful electron micrographs have been of such subjects as viruses, bacteria, flagella, and small muscle and tendon fibres. These are usually examined dried on a thin film of plastic. For larger objects it has been necessary to develop new methods of preparing very thin sections. The ordinary microtome will cut sections of 1–2 μ with difficulty; below this limit the plastic flow of the embedding medium prevents the knife from cutting. By using cutting speeds of several hundreds of feet per second, the knife blade being mounted on a high-speed flywheel, objects embedded in wax or camphor can be cut sufficiently thin for observation in the electron microscope. Artefacts produced in the specimen on drying, which denatures the proteins and destroys much of the characteristic structure, cannot be readily eliminated. "Freeze-drying" by the Altmann-Gersh technique is one possibility; here the material is frozen in isopentane cooled to −180°C and is dried by vacuum evaporation of the ice at −30 to −70°C under a pressure of 0·0001 mm. Hg. Attempts have also been made to mount the living specimen in an airtight cell, permitting it to be examined wet, though so far with little success.

Owing to the very low aperture of electron lenses their depth of focus is enormous—greater than the thickness of the specimen examined. There is therefore no "modelling" or depth effect in the photographs; overlapping fibres, for example, merely appear denser at the point where they cross. This difficulty can be overcome either by rotating the specimen holder and taking stereo-electronmicrographs, or by an elegant shadow technique which is becoming widely used. The object is placed in a high vacuum and obliquely bombarded with a rectilinear stream of heavy metal atoms. When examined afterwards in the electron microscope the deposit of heavy metal appears as a fictitious "shadow" reproducing very accurately the relief of the specimen. (Since the deposit of gold atoms represents the "light" and not the "shadow," it is usual to print the photographs obtained in their negative form.) A technique equivalent to that of histological staining is being developed. Normal stains are not significantly different in opacity from the rest of the tissue, but heavy metal compounds, preferentially absorbed at certain points in the structure, can be readily seen in the electronmicrograph because of their high density. There is a wide field here for further work on the intimate—one might almost say ultimate—structure of the molecular complexes present in biological systems.

Recovering from Tuberculosis

A CONVALESCENT patient, returning to the sanatorium after three days' absence on urgent business, said, "My friends are going to be my downfall, I can see." Bronzed, a stone heavier, and looking as if he had spent his year on a world cruise, he had been greeted with back-slappings (on his A.P. side), nudges (in his pneumoperitoneum), loud cries for drinks all round, and entreaties to make a night of it. It was a new experience for him to have to play the wet blanket; and he hated it. How long had he got to be "odd man out"?

No guarantee can be given to a convalescent tuberculous patient that he will never break down again. But if he can maintain good health with freedom from all signs and symptoms of active disease for five years he will be able to regard himself as "cured." The maintenance of good health will depend almost entirely on his observance of self-imposed restrictions; and five years is a large slice of life to spend walking delicately, especially for a person who shows no visible stigma of disease or disability, who feels well in himself, and who perhaps has social or economic reasons for wishing to conceal his true condition. The tests of graduated exercise at the sanatorium will have determined to some extent how much exertion he ought to undertake each day to begin with; and the rules of rest and relaxation will have been learned, practised, and acquired as habits—rules such as avoiding "getting out of breath," going to bed early, keeping statutory "rest hours" during the daytime, and, above all, resting whenever tired. These habits are easy enough to observe in a community where everybody else is observing them: it is when the patient gets home that his moral fibre is tested. How can he be helped? At this point it is essential to discover what circumstances brought about his illness. His work? His leisure? Or his whole attitude towards the business of living? This is a most important question, for on its answer depends his successful reablement—and prognosis.

Sometimes it is possible to contrive a change from an uncongenial job to one less exacting and more satisfying. But not often. As a general rule it is far better for the patient to return to the job he understands—so long as he does not positively detest it—than to switch to a new job with its new worries and uncertainties: a clerk is better advised to return to his office stool than to embark on the more hygienic hazards of poultry-farming. Naturally, at first he will only be able to engage in part-time work, and his hours should be arranged so that he arrives late and leaves early, thus avoiding the rush-hours on trams, tubes, and buses. Every effort should be made to enable him to lunch in comfort and to break his working hours with a proper "feet-up" rest during his lunch interval. With the present labour shortage, employers are more willing than ever to make such concessions, even for the less highly placed members of their staffs.

But the 40-odd hours per week spent at work are a far smaller source of danger than the 120-odd hours

Digitized by Google

of so-called leisure and the tensions caused by the many claims of interpersonal relationships during these hours. For many men and women life begins after the day's work is done. Shortage of help in the home spells a full-time burden for the home-maker. Can either husband or wife bear to lie with the feet up and refrain from lending a hand while the other is cooking, washing up, and getting the children off to bed? Yet this must be the rule for many months to come, and both husband and wife will have to face and accept the fact light-heartedly. The doctor can help to prevent emotional stress by forewarning the couple of this situation in all its details, and so to speak rubbing their noses in it. And there are also the claims of friendships and entertainments outside the home. Many men and women are dependent on their friends and fulfil themselves best in social pleasures. Are these to be abandoned? Clearly there must be a compromise. Life without visits from friends, occasional movies, or darts at the local may be so depressing as to undermine morale. Besides which, no patient must be allowed to "live for his disease ever after"—a tendency sometimes to be observed in the obsessional type who in pure culture will literally count his steps and order his life with a stopwatch.

Quite often it was nothing out of the ordinary in the patient's circumstances, but rather his attitude towards them—his modus vivendi—which produced his breakdown. This was what happened (we understand) to the writer of one of the two articles on tuberculosis in our Disabilities series.[1] All his life he had shown obsessional tendencies which led him into over-conscientiousness at his work and at his play. Not content with working at his own job during office hours he was always ready to shoulder those of others; moreover he got into the habit of taking work home with him and utilised the quiet small hours for paper-work instead of sleep. Meals became an unwelcome interruption and represented so many valuable hours wasted in cooking, table-laying, and washing up (for he was equally conscientious at helping his wife in the home) that he did his eating with one eye on the clock. His weekend gardening became a "fatigue," in both senses of the word, instead of a pleasurable recreation. He always had to be getting on with something. Idleness irked him: unless he complied with every condition in Kipling's *If* he could not regard himself as a man. And unfortunately this pathological attitude towards life, with its continual spur of depressing guilt-feelings, is regarded by the world as admirable and something to be encouraged—in other people. The addict also thinks it highly virtuous, and must be taught otherwise. Happily, mere common-sense discussion will usually do much for him, since, like Grosvenor in *Patience*, he is often very ready to change his ways if enough pressure is brought to bear from outside. His duty, of course, is to survive as long as he can as a wage-earner; and that will not be achieved by flogging himself along in a manner "the like of which he wouldn't treat a horse."

It will be seen that there are few hints and tips of a physical nature for the tuberculous, such as there may be for the one-armed, the arthritic, or the hemiplegic. The tuberculous patient has to *accept* his disability; which involves reaching a certain attitude of mind. The factors in his life which precipitated or contributed to his breakdown must be altered, as far as is humanly possible, by change of job, marriage with the right person, or the adoption of a quieter mode of living. But if the operative factors cannot be altered, his reaction to them must be changed. More often than not the months which the patient has spent withdrawn into a sanatorium have wrought a change by the time he leaves. Things have a way of settling themselves if given time; and for his part the patient has had ample opportunity for introspection, drawing up a spiritual balance-sheet, and determining his future policy. Should his problems be insoluble it is highly improbable that he will ever reach convalescence.

1. July 10, p. 75; Sept. 25, p. 507.

Annotations

THE PRENTICE PRACTITIONER

IN its report the first Spens Committee showed itself keenly alive to the value of an assistantship in the training of general practitioners, adding that "even those doctors who intend to become specialists would benefit from a year spent as an assistant in general practice."[1] Following the spirit, if not the letter, of the Spens recommendations, the Ministry of Health has put forward a scheme of grants to practitioners for training young assistants. It is proposed that any principal wishing to take an assistant for training shall apply for approval to the local medical committee, which is to consult two nominees of the neighbouring university. To qualify for a grant the practitioner must have at least 2000 patients on his list; he may not increase his list beyond the maximum that would be permitted if he did not employ an assistant under the scheme; and he may engage only one assistant at a time in this way. To benefit by a grant (which is restricted to one year) assistants must not previously have been in general practice in the British Isles except for short periods as a locum tenens.

The Ministry suggests that the principal shall receive £150 as a training fee, a sum not exceeding £700 for the assistant's salary and boarding expenses, and a car allowance of up to £150. These financial provisions do not satisfy the Insurance Acts Committee,[2] which objects that since the maximum number of patients is not to be increased in respect of the assistant in training, he is clearly to be regarded as a student rather than an employee (though this was not made clear when the figures first appeared). Yet from the £700—which will be passed on to the assistant, possibly with additions—the principal is expected to find the employer's contribution to National Insurance and superannuation, amounting in all to some £60; and the assistant would still have to pay his own contributions. The Ministry's reply is that a trainee should receive less than an experienced assistant, who, according to current advertisements, can expect £700–800 a year; and both the principal's and the assistant's contributions to insurance and superannuation would rank for income-tax allowance. Moreover, advertisements set an assistant's car allowance at £100, and the proposed maximum of £150 is generous.

This retort does not seem unreasonable. The £100 or so which, by the committee's reckoning, must come

1. Report of the Interdepartmental Committee on Remuneration of General Practitioners. Cmd. 6810. H.M. Stationery Office, 1946; p. 9.
2. *Brit. med. J.* Oct. 16, suppl. p. 140.

Digitized by Google

from the practitioner's own pocket or from the training fee has to be set against the probable advantages of securing twelve months' qualified assistance. Similarly, the young assistant should not resent getting slightly less than his seniors in similar posts, provided the year is spent in apprenticeship to a worthy master. Probably the number of established practitioners will considerably exceed the number of juniors wishing to avail themselves of the scheme. This should ease the local medical committee's task of ensuring that grants are paid only to principals willing and able to assume the rôle of tutor; and the presence on the committee of university representatives (which has been criticised as needless intervention) may relieve the embarrassment of eliminating claimants from a local group.

PSYCHOGENIC RHEUMATISM ?

"It is better to attribute incorrectly a small percentage of organic illnesses to functional causes than to condemn a large number of healthy patients to the fear of a non-existent disease." [1]

Prof. Philip Hench, of the Mayo Clinic, speaking on psychogenic rheumatism at the West London Hospital, on Oct. 12, was much of Dr. Armstrong's opinion. Pains which the patient calls rheumatic, yet which are not associated with organic evidence of rheumatism, are in fact "body language," he considers—mental pain and anguish experienced as bodily pain. The idea of a psychological factor in rheumatism is not new; indeed, Sydenham (as Dr. W. S. C. Copeman recalled) mentioned cases that, were it not for other factors, "might pass for a sort of hysteria." The question is whether the disease agent, whatever it may be, can ever be left entirely out of account. Taking the layman's definition of rheumatism as "any ache or pain within half a mile of a joint," Professor Hench thinks there are cases in which it can—cases caused entirely and primarily by fears and frustrations, and often confirmed by injudicious treatment ("iatrogenic fixation").

The rheumatologist can exclude osteo-arthritis and rheumatoid arthritis if their physical signs and radiographic changes are absent. Fibrositis gives more trouble, but also has specific characteristics. The patient with fibrositis tells a plain tale plainly: his pain is a localised ache accompanied by stiffness, causing fatigue, worse in the morning and evening and after rest, and affected by changes of weather; heat, physiotherapy, and salicylates relieve it for a time, but it can force its way to his attention through any distraction or preoccupation. The patient with psychogenic rheumatism tells a different story, and tells it in a tense defensive manner: the pain is indescribable, "like" so-and-so, or tingling, burning or stabbing, or it is a strange feeling; it is often not localised but felt "all over"; fatigue makes it worse, but it is often bad all the time, or worse at irregular times, not at the ends of the day or related to changes of weather, though often associated with emotional stress; heat and physiotherapy are quite likely to make it worse, and salicylates are usually ineffective; he forgets it when his attention is engaged but then he "pays for it later." Thus there are many positive evidences for a diagnosis of psychogenic rheumatism; and Professor Hench was able to offer one more: "when I find myself getting mad at a patient, I know that either I have a migraine coming on, or the patient has psychogenic rheumatism."

Dr. A. Spencer Paterson was unwilling, as a psychiatrist, to accept this massive gift of patients into his specialty; and put forward the claims of the rheumatic virus. The history, he said, often discloses evidence of rheumatic infection earlier in life—tonsillitis, chorea, or streptococcal infections. It may be that rheumatic infection has rendered these patients unfit for ordinary life, their mental symptoms being a result of rheumatism rather than its cause. The form which neurosis takes in a community is spread by suggestion, and possibly in America the favourite among patients just now is psychogenic rheumatism; but here, whatever may have gone on in Sydenham's day, our duty is still, he thinks, to try to apportion the blame fairly between the rheumatic agent and the trials and errors of the maladjusted victim.

1. Armstrong, T. G. *Lancet*, 1946, ii, 480.

SHEEP STREET

AN advertisement in our issue of Oct. 9 said:

"As a result of the recent death of a doctor on the Medical List of the Birmingham Executive Council there is a vacancy at 6, Sheep Street, Birmingham, 4, and 80, Great Lister Street, Birmingham, 7, for a doctor who wishes to undertake general medical services. . . . The owners of the properties are prepared to make available to the incoming doctor living and surgery accommodation, and the Council will require the doctor to live at the premises, No. 6, Sheep Street."

Admittedly, at the present time, most doctors entering general practice are glad enough to occupy any existing living and surgery accommodation. But in principle it is surely quite wrong that an executive council should insist that an incoming doctor must live at a stipulated address. The council has every right to require that the doctor shall live and practise near the patients whose care he agrees to accept; but any more precise condition seems hard to defend. However suitable and attractive the house in Sheep Street may be, it should not be made the only possible home for the new doctor. For a thousand and one reasons he may prefer the house next door or the rooms around the corner, and he should be allowed to exercise his reasonable choice.

In these times when traditional relationships in practice have been suddenly uprooted—when doctors are seeking new and non-financial ways of selecting professional colleagues, and ensuring amicable and effective coöperation in the health service—it is essential not to accept rulings that may later restrict our freedom of action, or our width of choice. While recognising that it is well within the competence of any executive council advertising a vacancy to state that it will give preference to a candidate willing to accept certain conditions of service, we cannot feel that it is in the interests of the community or of the profession that a council should lay down so definite a condition as to state the very house the doctor must occupy. In so doing it may incidentally restrict its own choice of applicants to those who allow themselves, by necessity, indolence, or inclination, to be herded to Sheep Street.

B.C.G. FOR NURSES

Dr. J. Heimbeck [1] has brought up to date his study of tuberculosis in nurses at the Ullevaal Hospital since 1924. In the first three years it was shown that the disease developed far more frequently among the Pirquet-negative than among the Pirquet-positive. From 1927 onwards the nurses were classified in three groups according as they were, at the beginning of their nursing careers, (1) Pirquet-positive, (2) Pirquet-negative, or (3) Pirquet-negative and thereupon B.C.G.-vaccinated. Of 501 vaccinated with B.C.G., 49 developed tuberculosis and 5 died of it. This gives 9·8% morbidity and 1% mortality. The Pirquet-negative nurses not vaccinated with B.C.G. showed, however, a 37·3% morbidity and 4·2% mortality from tuberculosis. Since 1932 Dr. Heimbeck has classified his B.C.G.-vaccinated nurses according as they did or did not become Pirquet-positive in response to B.C.G. By 1948 he could show that of 341 nurses rendered Pirquet-positive by B.C.G. only 19 developed tuberculosis, and only 1 died of it, whereas among 115 nurses who remained Pirquet-negative after

1. *Tidsskr. norske Lægeforen.* Sept. 15.

Digitized by Google

B.C.G. vaccination 27 developed tuberculosis and 4 died of it. (There remained 45 nurses not kept under close observation.) Thus a comparison between Pirquet-negative nurses who were not vaccinated and Pirquet-negative nurses whom B.C.G. made Pirquet-positive shows that the tuberculosis morbidity were seven times higher in the former than in the latter.

Heimbeck continues to prefer the Pirquet to the Mantoux test, which in his opinion tends to be too indiscriminately informative. He refers to the possibility of vaccination by the inhalation of B.C.G. in imitation of natural infection with tubercle bacilli; and, being much impressed by the benefits of accidental infection with virulent tubercle bacilli soon after B.C.G. has changed the Pirquet reaction from negative to positive, he looks forward to the time when such accidental infection will be replaced by carefully controlled intentional infection with virulent tubercle bacilli in order that the comparatively short-lived B.C.G. immunity may be replaced or substantiated by a more lasting immunity. His taste for the unorthodox induces a certain breathlessness in some of his colleagues, but the man who twenty years ago was regarded as very dangerous is now honoured as the father of B.C.G. vaccination in Norway.

ASEPTIC DISPENSING

THERE is nothing new in the idea of dispensing by an aseptic technique; for many years systemic injections and some drugs of low stability have been handled in this way. But the advent of penicillin gave fresh impetus to this branch of pharmacy, and nowadays the dispensaries of our larger hospitals regularly supply to the wards sterile solutions not only of penicillin but also of streptomycin, riboflavine, aneurine, ergometrine, water-soluble vitamin K, sex-hormone preparations, and many other drugs. The technique calls for a special laboratory or preparation room similar to that required by the regulations under the Therapeutic Substances Act (T.S.A.). Some of the smaller hospitals are still ill-equipped for this purpose; and the Ministry of Health has lately suggested that in such instances the resources of any nearby pharmacist licensed under the T.S.A. should be employed. The eventual aim must be to supply an aseptic service wherever sufficient demand is manifest. The Pharmaceutical Society, alive to the growing importance of this method, have pressed for the instruction of student pharmacists in bacteriology and aseptic procedures,[1] and today in most of the large towns the schools of pharmacy or technical colleges are holding regular courses in these subjects. In the early days of penicillin the Medical Research Council recommended that the hospital pathologist or bacteriologist should be responsible for its preparation. Now, however, this task is rightly regarded as within the province of the pharmacist. Nevertheless, the pharmacist should not be left to work in isolation. The aim is complete sterility, and the concept of "degrees of sterility" or of "relative sterility" should not be countenanced. The work of retail pharmacists engaged in this field is subject to periodical tests by the T.S.A. inspectors. A few have equipped themselves for actual bacteriological control at all stages; and all deserve any help that local departments of bacteriology can afford.

To some the aseptic dispensary may perhaps seem unduly elaborate, and it may be argued that the doctor's demands for sterile injections could be met from standard preparations. Certainly these are to be had in great diversity, but there remain the unusual dosage or combination, or other individual requirement which cannot be met in this way. Indeed, the increasing need for aseptic dispensing in retail pharmacy is reflected by the growth in the number of T.S.A. licences. Last October the number in England and Wales was 115: now it is 185. The pharmacist in a small way of business may object to the expense of equipping himself for this work; but comparatively cheap and yet satisfactory equipment,[2] and other ingenious devices by which the cost is kept down,[3] have been described.

1. *Pharm. J.* 1947, **158**, 125.

M.O.H.

THE duties of the medical officer of health are greatly altered by the National Health Service Act. Responsibility for local-authority hospitals, which was his, has been transferred to the regional board, while the clinical services which he administered will be controlled by the board or by the local executive council. At first sight it might seem that these changes reduce the interest and opportunities of the M.O.H.'s appointment; but at his installation, last Thursday, as president of the Society of Medical Officers of Health, Prof. R. H. Parry stoutly denied that this is so. "There is little doubt," he said "but that in the interest of preventive medicine many of these changes will be for the better. Much administration will be taken from the health department, and in consequence the medical officer of health will have more time to devote himself to his professional duties as a public-health worker." Henceforth the M.O.H.'s first task is to advise the local health authority on the removal of conditions impairing local well-being. It is not always easy to combine the functions of administrator and adviser, and thus the relief from administrative work should assist him in his advisory duties. Professor Parry proposes that in fulfilling these duties the M.O.H. should have the help of an advisory committee, whose findings should be made public. The public-health medical officer is now at a serious disadvantage in having no opportunity to visit the home and the family except as a sanitary inspector; and the old idea that he should be "independent of private practice" should be discarded. He should engage in work as either a private practitioner of social medicine or as a specialist epidemiologist, in each case with opportunities for research. At the same time clinicians should be encouraged to interest themselves in public health by gaining direct information about environmental conditions. The concept of social medicine can bring clinician and public-health worker into a single team; there will be overlapping, but this is so with any good team, for without it a gap is left open. All members of the team should meet from time to time at case conferences, in the interests not only of research but of the patient. Professor Parry, the declared enemy of the chair-borne, concluded: "Let those that are satisfied sit at the office desk and administer, but for the pioneering spirit there is still the open road."

OF DYING

Dr. Johnson preferred not to think about death, yet when his time came he made a good end. For most people this is a sound enough policy in dealing with an event as awkward as it is unpredictable; but doctors cannot stand aloof in quite the same fashion. They are obliged to give practical help to the dying, and they must know how best to do it.

In a symposium in the *Practitioner*[4] Lord Horder discusses the signs and symptoms of impending death, Dr. Hugh Barber the act of dying, Dr. W. N. Leak the care of the dying, and Dr. Leslie Banks euthanasia; and because dying ends fatally, Prof. Sidney Smith reviews the medical and legal aspects of death, and Mr. G. S. Lear some points about embalming and cremating. They read more lively than their subjects would suggest. Lord Horder warns against the deceptive patient who gets better after all—the typhoid patient, who has

2. Jackson, F. J. *Ibid*, p. 431; *Ibid*, 1948, **160**, 220.
3. Williamson, R. B. *Ibid*, 1947, **158**, 109.
4. August, 1948, pp. 73–107.

Digitized by Google

lain unconscious and pulseless for days and then reduces his slender chance by bleeding, and patients with congestive heart-failure, coronary thrombosis, or opium poisoning. He recalls, too, that a man may show advanced signs of a fatal disease without having any of the signs of *impending* death; and indeed, if the doctor divests his mind of the thought that the man's disease is incurable, he will find the accepted signs and symptoms of impending death to be extremely unreliable. We know more, Lord Horder says, about the act of dying than about death itself, and may be hard put to it to say when death actually takes place. He is quite clear about the doctor's duty when it comes to letting dying people die: there is little to be said for a physician who officiously prolongs for his patient the act of dying. Dr. Barber writes with experience of the reassurance and support which a good doctor can give to a dying man and his relatives. Belonging to the Johnsonian school, he is evasive when the patient asks whether recovery is possible—differing in this from Dr. Leak, who favours "a quiet straight answer with a clear look in the eye." Since the patient's preference in this matter is probably a matter of temperament, the best physician will be he who at the moment of test knows whether to answer as a Barber or a Leak.

Mr. Lear's tactful enthusiasm for embalming has a sound hygienic background, and he reminds us that a funeral director and his colleagues face some risk to health in their calling. The body of a tuberculous patient, or of a patient dying of sepsis, may endanger those whose task it is to prepare them for burial, unless technique is well designed and careful. The British Institute of Embalmers has established a research board to inquire into the possible dangers, to the living, from dead bodies; meanwhile funeral directors use their judgment about the need for embalming, regarding the process as a public service and providing it, when necessary, without regard to the financial status of their clients—a piece of public spirit not perhaps generally recognised.

ŒSTROGENS IN DIABETES

ALTHOUGH insulin is specific in the treatment of diabetes there is evidence that some extrapancreatic endocrine factors may augment its effect and reduce individual insulin requirements. Marcus and Glotzer[1] report a reduction in the severity of diabetes in post-menopausal patients treated with œstrogenic hormone. In the 7 bedridden subjects chosen, aged 62–77 years, diabetes had either been present before the menopause or had been aggravated by it. An adequate control period before treatment is essential, and the diet and insulin requirements of these patients were unchanged during a preliminary observation period of at least five months. After this, 6000 rat units of œstrogenic hormone ('Progynon B') was injected intramuscularly twice weekly for three months. A fall in daily insulin requirement of 25–50% was observed in 4 of the patients. There was also an almost precipitous fall in blood-sugar in 6 of the patients, after four weeks in 5 cases and at the seventh week in the remaining one. All the patients noted a "remarkable feeling of well-being," and only one had uterine bleeding.

Œstrogenic hormone may exert its effect indirectly by depressing the secretion of diabetogenic hormone by the anterior lobe of the pituitary; this view is supported, for example, by Biro's[2] recent report in these columns of symptoms of hypoglycæmia in patients receiving stilbœstrol. However, in previous studies of the nutritional aspects of diabetes, with particular reference to the liver, Biskind and Schreier[3] found in 94 diabetics not only signs and symptoms of vitamin-B complex deficiency but also syndromes related to excess œstrogen. Intensive nutritional therapy benefited most of these cases, suggesting a correlation between the lesions of nutritional deficiency and impairment of the œstrogen-inactivating mechanism of the liver. These results conflict with the other work mentioned above, but further carefully controlled clinical trials may show, as Marcus and Glotzer hope, that in suitable cases œstrogenic hormone therapy has a place as an adjunct to, or substitute for, insulin.

1. Marcus, H., Glotzer, S. *N.Y. St. J. Med.* 1948, **48**, 1461.
2. Biro, G. *Lancet*, Sept. 25, p. 513.
3. Biskind, M. S., Schreier, H. *Bull. N.Y. Acad. Med.* 1945, **21**, 436.

WAR CASUALTIES

THE Ministry of Pensions' year-by-year account[1] of war casualties, with the varying proportions between the Forces, the Mercantile Marine, and the Civil Defence Services and civilians, reflects in grim outline the actual course of military events. It also reflects a growing sense of obligation to those killed or injured in war. In progressing by short stages it is easy to think that we are hardly moving at all; but by compressing its story of the last nine years into a single report the Ministry shows that step by step we have travelled far from the outlook of 1939. Whereas then the minimum payment to a severely disabled pensioner who had married after being disabled, and had two children, was £1 12*s*. 6*d*. it is now £5 11*s*. Increases derive partly from an improvement in pre-existing allowances, and partly from fresh supplements such as those for unemployability and special hardship. The most notable change of principle in the reckoning is the acknowledgment that a wife married, or children born, after disablement should count for allowances. With increase in their amount, there has been a parallel relaxation in the rules governing the grant of pensions. Thus in 1943 it was laid down that no onus to prove his case should rest on the claimant, who was to have the benefit of any reasonable doubt. Though refusing to accept the principle expressed in the slogan "fit for service, fit for pension," the Government ruled that a Serviceman invalided with a disability not noted on entry to the Forces should receive a certificate of entitlement in the absence of evidence that the disablement was not related to service. This has opened the way to thousands of successful claims which previously would have been rejected.

In these and other changes successive Governments have sometimes led, and at other times followed, national opinion. Wherever the credit may lie, the movement is in the right direction.

THE DISTINCTION AWARDS

THE third Spens Committee recommended that "distinction awards" in three grades should be made to consultants and specialists in recognition of special contributions to medicine, exceptional ability, or any outstanding professional work (other than administrative). These awards, it was suggested, should be made by "a national committee consisting in the main of eminent members of the profession who from their own knowledge or otherwise would be able to reach an authoritative opinion on the comparative merits of candidates." The Ministry of Health last week announced that the Government, in reviewing the Spens report, have decided to set up such a committee, and that its constitution has been settled after consultation with the Royal Colleges and Scottish Royal Corporations. "Invitations to the individual members," it is stated, "will shortly be issued," and a full announcement will be made when the details have been completed.

WE regret to record that Mr. PERCIVAL COLE, consulting surgeon to the Royal Cancer Hospital, London, died on Oct. 19.

1. Ministry of Pensions: 23rd Report, for the period April 1, 1939, to March 31, 1948. H.M. Stationery Office. 1948. Pp. 45. 1*s*.

Digitized by Google

Special Articles

THE STRUCTURE OF MEDICINE

DR. WALSHE'S HARVEIAN ORATION

THE annual Harveian Oration was delivered at the Royal College of Physicians last Monday, St. Luke's day, by Dr. F. M. R. WALSHE, F.R.S., who took as his subject the Structure of Medicine and its Place among the Sciences.

Commonly, he said, the intellectual structure of medicine is expounded in terms of two pairs of antitheses —namely, art and science, observation and experiment. Thus the relative scope and limitations of observation and experiment are treated, not as they should be, in terms of experiment as one mode of observation, but as though the two terms expressed a thorough-going dualism in scientific method. A comparable distortion usually informs the comparative consideration of the rôles of art and science, and many an empty argument has been held on whether medicine is the one or the other. In fact, all these antitheses arise from the unguarded use of abstraction. To achieve a philosophy of medicine it is necessary to escape from the fragmentation of ideas that comes of thinking too exclusively in the static terms of classifications; more thought should be given to the idea of process.

MEDICINE AND PHYSIOLOGY

Some physiologists, said Dr. Walshe, would deny medicine its place among the sciences, and speak of it as nothing more than applied physiology. Historically, such a claim is easily refuted, for the hospital is the cultural ancestor of the laboratory, and experimental physiology was born of therapy. Implicit in the physiologist's argument is the thought that medicine does not carry its analysis of phenomena back to fundamental notions, but stops at a half-way house where it meets and tends increasingly to borrow from other sciences. Yet here medicine is no exception amongst the biological sciences; and indeed physiology has been eagerly borrowing from the other sciences for the past hundred years. The truth is surely that every successive layer of thought in the analysis of nature, living and dead, stops at a half-way house when tracing its ideas back to their basic elements, and is content with ideas of a generality sufficient for its immediate purpose. For philosophy alone, which aims at supreme generality, there is no half-way house.

Some generality of understanding is the essence of a civilised culture; the medical professions must seek it if they are not to decline to the level of craftsmen and technicians. This danger is real; and the many proposals for reform of medical education designed to avert it have been superficial and uncoördinated.

OBSERVATION AND EXPERIMENT

In observation, Dr. Walshe continued, what is retained is retained in a subjective order of importance, and thus there is some distortion of the impartial facts. The term "trained observer" acknowledges that observation is discrimination and not a product of pure sense perception. All observations are subject to interpretation in terms of concepts; the notion of pure knowledge as the product of pure sense perception corresponds to nothing in human experience. There is a constant interplay between the conceptual and the observational order of experience. New observations modify concepts; but, not less, new concepts lead to fresh possibilities of observation. The mind that observes is also the same that devises, performs, and interprets experimental observations; for experiment is but a method of providing observable data. Thus no higher order of rationality attaches to experimental observation.

In medicine, the data, often very incomplete, are taken in all states of refinement. They have to be sorted, translated into the language of medicine, expanded by analogy, logically interpreted, and finally made to emerge as clearly formulated propositions, and as exemplifications of laws of nature. It is because important data are so often lacking that recourse is commonly had to the method of experiment. The ultimate aim of the scientific observer is to grasp the principles inherent in the stream of evanescent phenomena; and by experiment he seeks to isolate his material to make it reveal its principles. In the words of A. N. Whitehead, "experiment is a way of cooking the facts for the sake of exemplifying the law." Experiment thus provides a double clarification: the formulation of an abstract principle, and the exemplification of it in as simple and unequivocal a medium as possible. Clearly an even higher degree of abstraction is involved here than in simple observation. This is perhaps why the experimental method, exclusively pursued, may prove narrowing to the mind; it may also account in a measure for the ill-disguised hostility of many experimental scientists to metaphysics. "Action is easier than contemplation." Nevertheless, no fundamental distinction separates observation and experiment. In both there is a concentration of attention upon specific phenomena, and also some control of events; and both seek to provide data for interpretation.

In medicine there is too great a readiness to equate the notion embodied in the word "experiment" with that of "animal experiment," and to think of experiment as something divorced from the bedside. Simple experiments are prevalent in day-to-day clinical studies.

> "Every time we evoke an extensor plantar response . . . every time we elicit a knee-jerk, we are forcing certain spinal mechanisms by their mode of reaction to reveal internal conditions in the central nervous system that unaided observation by the five senses cannot tell us of. We are controlling conditions and isolating our material by a method that has all the essential form of the experimental method. . . . The hospital ward is a laboratory in the fullest sense, is indeed the parent of all biological laboratories."

ART AND SCIENCE IN MEDICINE

In discussion of art and science in medicine some lean too readily to hard antithesis, for the continual tendency is for the practical arts to be converted into applied science. In theory this is understandable, for the practical arts are operations according to rule, and rules are general propositions referring to particular cases and directed to future situations. Thus the rules of a practical art are predictions to be tested and validated by prescribed procedures. In this may be seen the slow development of science in medicine—the emergence of ideas from activities, and the influence of these ideas in rationalising and modifying the activities from which they emerge. As to the term "applied science," it is well to remember that this cannot be applied in medicine to the fruits of scientific discovery irrationally employed.

Turning to the intellectual arts, Dr. Walshe said that here the problem becomes not that of art *and* science but that of art *in* science. The physician seeking to be scientific attempts to transform the confused data of direct experience into the clearly formulated propositions of a rational science, and to identify the patient's situation as a particular example of the relevant natural laws or general principles. The accomplishment of this is essentially a special example of the use of the liberal arts. "For the trained mind every complex of presenting phenomena is a text to be read, translated into the grammar of science, rhetorically expanded, and logically interpreted." Signs and symptoms are grouped into

Digitized by Google

patterns and sequences, thus clarifying what may be termed their space-time relationship; and from the patterns discerned on examination and the sequences observed over a period of time, the future course of events is predicted. But the original data are considered in the light of further terms—those of physiology, pathology, and ætiology. These are studies by the methods of science; and the gift of insight, the ability to discern and develop analogies, to detect patterns and sequences, and to interpret logically, constitutes artistry that is an integral element in scientific activity at its best.

CONCLUSION

It may be urged, said Dr. Walshe, that this examination of intellectual machinery simply complicates a process normally taken in the stride. Such criticism is more likely to come of intellectual sloth rationalised as practical common sense or from the comforting persuasion that freedom to think implies also freedom not to think, than from any deep conviction that each can do his best without knowing something of how he does it. The capacity to advance knowledge materially and to develop a due critical faculty are both impossible on the plane of "practical common sense."

> "Further, I ask how medicine can be worthily taught on its academic side unless by minds well versed in the liberal arts . . . understanding the principles on which knowledge is ordered and capable of expounding and of showing in action the reasoning methods involved."

In conclusion Dr. Walshe said:

The need for rebuilding the foundations of medicine was never greater than today when we are being swept along on a spate of new knowledge and new techniques, and have so little time for their due contemplation and integration. Surely there could be no function more truly appertaining to our traditions, or more in harmony with the life of that great natural philosopher whom we commemorate today, than to seek to study and to consolidate these intellectual foundations, and to further what I have called a generality of understanding.

If some philosophy of medicine does not find a home amongst us, where shall this be found? Not, it is increasingly apparent, in the modern university, nor in a Ministry of Health; and if we do not show ourselves eager to promote such a philosophy, then the sum of our corporate activities as a college, whatever their immediate importance, becomes trivialised.

History does not record what book it was that William Harvey was reading, as he sat under a tree with the two young sons of Charles the First at the battle of Edgehill, but we may be sure that it did not deal with consultant services nor with the pay and grading of specialists.

The vigour of such a society as this college can be preserved only for so long as we actively and corporately cherish and foster intellectual ideals. All vigorous societies cherish aims over and above the safe provision of the material necessities and gratifications of their members, and once we allow these to dominate our conscious aims, decadence will have already marked us for its own.

The world in which we live has seen more change since Harvey's day than did the millennium before him. His exhortation "to search and study out the secrets of nature by way of experiment" now has implications he could not have foreseen. Research today within our science is the purpose of large organisations with vast budgets at their command, and its guidance and inspiration have outranged our capacity and slipped from our grasp, for reasons some of which have been beyond our control. Nevertheless, no loyal sons of this ancient college will be willing to allow that we are left without a worthy purpose. This college can, and, if it is to survive as something significant in the intellectual life of medicine, must remain a fountainhead of academic medicine, of true learning—the home wherein a philosophy of medicine finds a permanent abiding place and disciples eager to learn and to teach it, and where the liberal traditions of medicine can look confidently for their defence against the constant threat of debasement by the technical arts and by the spiritually and intellectually oppressive materialist dogmas of our day.

THE TRANSVAAL HOSPITALS DISPUTE

FROM A SOUTH AFRICAN CORRESPONDENT

MANY of the arguments lately heard in Great Britain have been aired again in the Transvaal province of South Africa, where doctors are involved in a dispute with the Administration over the proposed introduction of a free hospital service. So definite and irreconcilable are the opinions of the disputants that honorary staffs in the hospitals of the province have refused to operate the proposed scheme, and consequently the hospital service is disrupted and is deteriorating rapidly.

Hospitals had for many years been financed and organised out of public funds, but had been staffed on the "voluntary" plan with interns and honorary surgeons and consultants. As a new measure of social service a recent ordinance of the Transvaal Provincial Council proposed that all hospital treatment should be completely free, and to this end new salaried posts should be created in the hospitals, which it was hoped that the present honoraries would apply for and accept. The South African Medical Association felt that a completely free service was not desirable, and suggested that a means test should be applied. This suggestion met with no sympathy from the Transvaal Provincial Council, which maintained that the ordinance expressed the will of the people.

Both sides made emphatic public statements. The S.A.M.A. maintained that the new ordinance would bring about increased demand on the hospitals and hence lack of accommodation for the adequate treatment of the sick poor; that it would endanger the livelihood of the profession; and that by allowing free medical treatment to those who could afford to pay it would upset the whole foundation of the honorary system. The Administration replied that a system of hospital care paid for by taxation would remove the dread of financial embarrassment that serious sickness means for the middle-class patient; that there would always be enough remunerative work for doctors even under the new system; and that the authorities were fully prepared to pay for medical services rendered under the ordinance.

The dispute dragged on. On Oct. 1 the new ordinance came into force. The doctors did not apply for the new salaried posts, but proposed attending inpatients in the hospitals for a further fortnight as a period of grace. They also proposed mediation, which the Administration would not accept. On Oct. 2, when negotiations seemed to have broken down, the S.A.M.A. issued a directive that all honoraries should cease acting immediately, provided that, if they were permitted access to the hospitals, they should continue treating patients admitted before Oct. 1, and that emergency cases should be treated if specially requested by the medical superintendent. At the same time the S.A.M.A. reiterated its previous demands, and the Administration repeated that it could not accept these demands.

While this action was designed to safeguard at the same time the patients' interests and the doctors' rights, it inevitably curtailed the hospital services and largely shocked public opinion. In most hospitals emergency arrangements were made with the staff available. Outpatient departments were generally closed and bewildered "regulars" were turned away. Casualty departments functioned, but patients requiring ward treatment were put on a waiting-list. As patients left hospital and very few new ones were admitted, beds and wards rapidly emptied. The Transvaal newspapers published photographs of operating-theatres standing unused, and there was much mention in the press of the Hippocratic oath.

The Transvaal Provincial Council then announced its intention to take a referendum, asking the public to

Digitized by Google

decide whether a means test should be applied to the hospital scheme or not. There seems to be some doubt as to the legality of this step—which is unprecedented in the Union—and the council have since deferred action, while again discussing the possibility of the appointment of a mediator acceptable to both parties. Whether either side is now prepared to accept—by referendum or mediation—a solution contrary to its own proposition is somewhat doubtful.

Johannesburg interns have stated that they cannot carry on with work outside the range of their experience without the guidance of the honorary staff. In this statement they have since been supported by the interns of other hospitals in the Province. So the dispute goes on with statement, ultimatum, and counter-statement.

POLIOMYELITIS IN NEW ZEALAND

FROM A NEW ZEALAND CORRESPONDENT

IN New Zealand the conduct of operations against serious epidemics is on national lines instead of being left in the hands of the medical officer of health according to the needs of the district. And mass restrictions have always been more popular in the Antipodes than in Britain. So when poliomyelitis descended suddenly on Auckland last November, producing 26 cases within a fortnight, a ban was placed on all gatherings of children under sixteen throughout the Dominion, and on their travel between the two islands. The interference with education, and the dislocation of normal community life at Christmas, were serious, and by March it was obvious that the bans were no longer serving any useful purpose even if they had originally done so. Accordingly the official policy was changed in favour of closure of the particular school affected. By this time the epidemic was running at some 13 cases a week, and it has since continued throughout the winter, with seldom less than 20 cases a week and with the Auckland province still providing the highest incidence.

The Wellington health district has never been immune, but there were not very many cases till recently when the disease showed evidence of rapid spread, attaining 72 notifications in September. The reopening of the schools was therefore postponed. But the Royal Australasian College of Physicians, meeting in Dunedin, passed a resolution for the consideration of the minister of health that "there is convincing evidence from epidemics elsewhere that the general closure of schools has had no influence on the spread of the disease or its severity," and "at this stage of the epidemic no useful purpose can be served by the general closure of schools," adducing as evidence of this the very high rate of abortive cases among both adults and children. The minister accordingly announced a new approach to the problem. Children were to wash their hands before eating, parents were to provide them with towels, and teachers were to see that excessive fatigue was avoided, to wage war on flies, and to conduct a morning health inspection, reporting any suspicious symptoms to the district health office.

Now the newspapers have just described a report by Dr. A. W. S. Thompson, medical officer of health at Auckland, tabled in the House of Representatives as an appendix to the annual report of the department of health. He and his colleagues investigated fifteen areas, each of about twenty houses, where the first cases of poliomyelitis occurred, and noted the incidence of minor illnesses consistent with a diagnosis of abortive poliomyelitis. (For purposes of comparison a similar inquiry was made in areas on the other side of the harbour where no cases had been notified.) The ratio of suspect illnesses to positive cases proved to be about 300 to 1, and on this basis the true number of cases in the Auckland outbreak has been about 40,000 in nine months.

REFRESHER COURSES FOR GENERAL PRACTITIONERS

MINISTRY'S ARRANGEMENTS

THE Ministry of Health has set out in a memorandum (G.P.R.C.1) the Government's scheme for grants under the National Health Service Act to practitioners in the National Health Service who attend refresher courses. The memorandum also defines the conditions on which doctors engaged in general practice before recruitment to the Forces may apply for a similar grant after demobilisation.

Practitioners in the Health Service.—The courses for attendance at which financial assistance is offered are those specially arranged for general practitioners by the universities and medical schools. A practitioner taking part in the N.H.S. can claim grant for attending one course of 22 half-day sessions or two of 11 half-day sessions (which may be either intensive or spread over a number of weeks), provided that:

1. He has been qualified for at least three years.

2. He has not less than 500 (or in a rural practice 250) people on his list. In the early days of the service, however, a minimum of 300 (or 150 in a rural area) may qualify.

3. Within the previous year he has not received financial assistance under the Government schemes for doctors released from the Forces, or for N.H.I. or N.H.S. doctors. Exceptionally this condition may be waived.

Application for admission to a course and for grant should be made on form G.P.R.C.2 to the university, which, if prepared to accept the applicant, will forward the application for grant to the Ministry. The Ministry will then inform the doctor, the executive council, and the university whether the application is approved. A doctor qualifying for grant is normally not concerned with payment of the course fees. The following expenses may be reclaimed by those qualifying: (1) subsistence allowance up to £1 a day, if attendance necessarily entails absence from home at night, or otherwise actual expenses up to 5*s*. a day; (2) travelling expenses; and (3) payment of a locum tenens where necessary, up to a maximum of 14 guineas a week.

Details are given in the form of claim (G.P.R.C.3) which should be completed at the end of the course and sent to the postgraduate dean or director who, after certifying that the course had been attended, will forward it to the Ministry for settlement. Copies of application and claim forms are obtainable from postgraduate deans or directors.

Ex-Service Practitioners.—Broadly the arrangements for practitioners released from the Forces are the same as those for doctors in the N.H.S. Ex-Service doctors, are, however, given the option of returning to their medical school, where they may select the instruction they most need; and in this event they can claim reimbursement of fees up to a maximum of 10 guineas for 22 sessions. The conditions on which grant is made to the ex-Service practitioner are that:

1. He applies within a year of demobilisation.

2. He has not within the previous year received financial assistance under the Government schemes for doctors released from the Forces, or for N.H.I. or N.H.S. doctors. Exceptionally this condition may be waived.

Any ex-Service practitioner satisfying these conditions, and accepted by the university, automatically qualifies for grant; the Ministry's prior approval is not required.

Digitized by Google

Disabilities

15. DEAFNESS

THE general public does not understand deafness, largely I surmise because it attracts little attention and does not evoke sympathy to the extent that blindness does. The reaction of most people when told that I am deaf is to shout in my ear; and on being told that this is useless, that I lip-read with great difficulty or not at all, and would they please write their question down on paper, they walk off. Nor is it appreciated that hardly two cases of deafness are alike. Each has its peculiarities. There is every grade of deafness from very slight to complete, and these grades are further differentiated by whether the deafness be from birth, early childhood, later childhood, adolescence, maturity, or old age. On top of this is the mental capacity of the deaf person and his attitude to life; this last is more important than anything in determining whether deafness is to be an insuperable obstacle or not.

I became totally deaf in 1915 as the result of cerebro-spinal meningitis, when I was 13. I believe I had exceptionally sensitive hearing before that, for I could pick out with ease the various voices singing in harmony, and too close a proximity to fireworks would temporarily deafen me. For two days I was delirious, and my first impression on waking was that the large building opposite my bedroom had been transformed into a war factory, for I could hear machines buzzing, hammers clanging metal on metal, and steam escaping from valves. I was speedily undeceived by my mother writing to me on a slate, for she had already discovered that I was deaf.

The noises I heard were, of course, tinnitus, and they have persisted ever since; so it is erroneous in my case to describe myself as living in absolute silence. On the contrary, a bigger medley of sounds than I can describe accompany me willy nilly, though I have long since learnt to ignore them when my mind is otherwise occupied. Submitting to the fact of total deafness, as I must, I am rather glad than sorry that I have these head-noises, for I find it pleasurable at times, and even profitable in a sense, to bend them into a tune remembered from my hearing days or composed impromptu. The various sounds accurately fit instrumental music. In this purely subjective manner I can "hear" music at will; perhaps Beethoven, who was for years stone deaf, composed in this way!

Almost complete loss of balance accompanied the onset of my deafness. It took me fully six months to learn to walk reasonably straight in daylight; and only by walking swiftly could I keep a fairly straight course in the dark, and then only by having something visible —a lamp or a lighted window—to steer by. A turn of the head to speak to a companion would upset my balance and make me wobble about like a drunken man. Even now, I cannot walk straight in complete darkness.

A further peculiarity was (and is) that whereas before my deafness my field of sight remained at a constant level, it now went up and down with the movements of my head. At first this was a nuisance, but it has become somewhat modified with the passing of the years, though it is still noticeable when the head is involuntarily jerked as in vehicles passing over bumpy roads.

These were the subjective results of total deafness in my case; but they were not the most important effects. It was at once forced on me that deafness means isolation from the normal world. It was uncanny after about three months in and out of various hospitals and convalescent homes to revisit the scenes of my recent hearing life, to meet my former class-mates, to watch the heavy streams of traffic in the West End, and yet to hear absolutely nothing. Vibration could be, and still is, felt; but only from heavy vehicles, or from footsteps on wooden floors.

Being cut off from one's fellows by an invisible and ever-present barrier is the heaviest blow and disability of deafness. My friends knew nothing about it; only personal contact with me could have taught them, and that personal contact I dreaded. There was a constant tendency to withdraw as far as possible from intercourse with the outside world, and obviously if this had been allowed to go on unchecked mental instability would have resulted. Even so, my speech began to suffer through lack of use. I became more and more tongue-tied, and when I did speak I gabbled. Normal folk had difficulty in understanding what I said.

I can hear my own voice perfectly—even a whisper sounds loud—but I know that to hearers my voice has the characteristic deaf tone. I can also sense a difference in my voice according to the size of the building in which I am speaking; but whether this is based on reminiscence or not I cannot say.

* * *

Such then were the general conditions with which I, at the age of 13, had to face life. At first I was somewhat buoyed up by the repeated statement that in time my hearing would return. It did not, and I am now aware that deafness resulting from meningitis is virtually for life. Six months later I went to a deaf school, and at about the same time I entered what is known as the "deaf world" by joining in the activities of the Royal Association in Aid of the Deaf and Dumb —otherwise I might well be mentally ill today.

Though I had become totally deaf so young, I had one great advantage over the born-deaf and those who become deaf even earlier than myself—I could read with profit. On that apparently simple fact, coupled with my entry into the "deaf world" everything hinged. It was a cardinal point. At the deaf school I simply could not lip-read. The ability to lip-read is a gift. You are either born with it or you are not. Out of the hundreds on hundreds of deaf people whom I have met, very few can be called genuine lip-readers, and I know no lip-reader at all who can follow a normal speaker at a lecture. Those without the gift can try for years and never get beyond mastering the ordinary phrases "How are you," &c. But I could read.

It was clear that I should have to educate myself solely from the printed word. There is a saying: "The eye for the ear, and the hand for the tongue"; and it illustrates the truth that for the deaf all knowledge must go in through the eye, and much of it must be spoken on the hands by using the manual alphabet or by signs. My communication with the non-deaf world is almost entirely by means of pencil and paper. If my school-teachers wished to tell me anything they had to do it in writing, for some refused to spell on their hands. If my employer wished to give instructions he too had to put it on paper; I found this rather an advantage, for if any mistakes were made I could verify what I had been told to do. I cannot say that I found total deafness a disadvantage as a silversmith. On the contrary, the fact that I could work at a delicate job amidst terrific dins was a great help, and I took full advantage of it.

Meanwhile for a decade I had been living in the deaf world. Nearly all my former hearing friends had long since dropped out of my life; but in their place I had made contacts with deaf ones, and was taking part in a normal social life with them. In this way my own deafness became, as it were, normal.

I suppose I am one of the few totally deaf men to have been through a college. I was allowed by the authorities at King's College, London, to take their theological diploma. The same could be done by any deaf person provided they can read with profit. I attended lectures,

Digitized by Google

not to listen, for I couldn't, but to copy notes from friends as I sat beside them. In that way, and by borrowing other notes, I probably obtained a better record of a lecture than the normal student. The notes, coupled with the careful study of recommended books, enabled me to hold my own. After all, this is much the same as taking an external degree. For many years now I have been employed as a chaplain and worker for the deaf, and have met thousands of all types. Our classification is generally this: the born deaf, or the deaf and dumb; the deafened, those who suffer from more or less severe acquired deafness; and the hard-of-hearing, who with an aid can retain their place in the normal hearing world.

For the first two classes the greatest disability caused by deafness is the isolation and cutting-off that I have described. The disability of having been born deaf, though it has the inevitable consequence of retarding education to a degree quite unrealised by the public, is less of an affliction than acquired deafness, for the born deaf never know what they miss.

Where deafness is incurable, either from birth or afterwards, the only way to a normal life where the disabilities of deafness can be forgotten is to take an active part in the social life offered by the welfare agencies. In spite of the many things that a deaf person can do as well as the normal, deafness remains a formidable handicap. The Disabled Persons Act and the new National Assistance Act may do much for the likes of me. A regular job, freedom from anxiety, and an interesting social life are needed if the results of deafness are to be side-tracked.

Public Health

Mobile Maternity Centres

THE Ministry of Health, in a circular (161/48) to local health authorities, suggests the use of specially equipped vehicles for the examination of mothers and young children in remote areas. These mobile centres could be used as adjuncts to waiting-rooms hired periodically, or for conveying the equipment needed to convert rooms temporarily into a maternity and child-welfare centre. The Minister also urges the formation of further mobile dental clinics.

Poliomyelitis in the U.S.A.

The poliomyelitis epidemic in the U.S.A. is now believed to be past its peak. In the week ended Sept. 25 the number of cases reported was 1609, compared with 1840 in the previous week. The five-year average for the corresponding week is 881; and in 1946, the last big epidemic year, there were only 1425 cases. The decline, says *B.U.P.*, has come later this year than in 1946, and the cumulative total of cases for the year up to Sept. 25 is higher—17,653, compared with 17,206 in that year. Between March 20 and July 24, 59% of all cases were recorded in North Carolina, Texas, and California; the present fall is sharpest in the north central States.

The Second Quarter

The following vital statistics have been reported for the second quarter of this year:

—	Births		Deaths		Infant mortality per 1000 births
	No.	Annual rate per 1000	No.	Annual rate per 1000	
England and Wales	203,711	19·0	110,356	10·3	31
Scotland	26,554	20·7	14,695	11·4	43
Northern Ireland ..	8030	23·9	3821	11·4	44
Eire	18,006	23·8	9419	12·5	46

In England Now

A Running Commentary by Peripatetic Correspondents

IN the course of several years of psychiatric practice I have regarded the term "trick-cyclist" at first with suspicion, later with tolerance, and finally with affection. It is a kinder appellative than many that come our way; it at least suggests that one is capable of performances requiring unusual balance and poise. It came, however, as something of a trauma to be confronted with the real article, a being who literally trick-cycles for his bread and butter. Referred by his M.O. as a case of anxiety state, Sydney was a tremulous sweaty weed of a youth who laid claims to "blackouts" for as long as he could remember, if not longer. He had always been too shy to play with other boys, and his dad had bought him a motor bike "to bring him out of himself." The desired social effect was apparently not forthcoming, and dad, perhaps in despair, had gone off with The Other Woman. Having now a mum as well as a motor bike to care for, young Sydney very creditably sought more gainful employment. Came the local fair and our hero found himself gazing at the "Wall of Death" with a wild surmise. Modestly he offered to reinforce the small staff of two, the Boss and the Lady. Surprisingly he was accepted.

At that time he was averaging three blackouts a day, but for several weeks he contrived to have them in lavatories, peep-shows, pubs, and secluded gutters, and to keep his art pure and uncomplicated. It took him but five minutes to learn that his trade really amounted to no more than a steady 20 m.p.h. jog, the impression of spectacular speed being contributed by the small circumference of the wall, and the incredible horizontality of the whole affair resting entirely with that mysterious but ubiquitous agency, centrifugal force. He was permitted to graduate to steering with his feet on the handlebars; but the Lady's tour-de-force of standing on the saddle was strictly copyright.

Inevitably, however, he was discovered blacked-out and prostrate, and was summarily dispensed with as being liable to make the wall altogether too deathlike. Subsequently conscripted, he was classified as unsuitable for dispatch-riding, much to his dismay. As a mess orderly he was obliged to remain vertical for as much as an hour at a time. Accordingly he showed an increasing tendency to regress to a horizontal, though unconscious, similitude of his earlier state.

I wonder if they call trick-cyclists "psychiatrists" nowadays?

* * *

A visit to the Jackson Laboratory for the Study of Animal Behaviour, Genetics, and Cancer, at Bar Harbour, Maine, confirms one's belief in the phœnix. Last year some careless workmen left an incinerator fire before it was properly extinguished, and it spread into the peat soil, eventually defying for ten days the efforts of thousands of people and a score of fire brigades. The main building was in the centre of the conflagration and was burned out, and nearly all the mice inside were burnt or suffocated by smoke. The visitor now sees an untidy sort of compound, or barrack square, with a few poles and triangles embedded in it, surrounded by the charred stumps of felled trees. At one corner stands the one remaining wing, which was fireproof, covered with wooden scaffolding (this is pine-tree country), with a new roof being finished, and adjoining it a new wing, now almost complete. At the other side of the square there are three large wooden bungalows which house the summer school. For this there is an enrolment of some thirty students, who range from college freshmen to candidates for master's degrees. In addition, a dozen or so summer investigators of PH.D. status come up for a few months to work with the incomparable material of the Jackson Laboratory or to escape the heat of the cities farther south and write in peace and quiet. The stakes and triangles are the real skeleton of the phœnix. The new building, when it is completed next year, will have an auditorium, a library, offices, a histology and a biochemistry laboratory, and an electron-microscope room. The old section will only house the mice, which are already back in their thousands. Nearly all the known genes have been reassembled from all over the world.

Digitized by Google

At Hamilton Station, eight miles away on the other side of the town, there is now another laboratory. Instead of mice, here is a profusion of rabbits and dogs, with a few cats whose coat-colour inheritance is being studied. The rabbits are being selected for anatomical anomalies and malformations, such as extra ribs and vertebræ and patent foramen ovale; it seems that most human abnormalities have their counterpart in these animals. The dogs are of several pure breeds, and the main work concerns behavioural matters—whether, for example, a litter of pups from a normally staid breed becomes more playful if brought up by a mother of a playful stock. The visiting investigator is overwhelmed by the two chief features of the laboratory: the enormously valuable material, enough to keep a score of embryologists, histologists, and pathologists busy for years; and the hospitality and group feeling of the staff, which would induce the visitor to sign on every year as a summer investigator if only he could.

* * *

He was a silvery-haired fresh-faced English surgeon, who always travelled abroad in a plum-red corduroy suit and green bow tie—the picture of glorious Technicolor. His knee-length R.A.F. boots completed the ensemble. As spring broke through he reached Bratislava. "Tonight ve shall dine in se Café International," announced his host. As they entered the café—a lovely subterranean mid-European "wein-stube," complete with alluring alcoves—the orchestra instantly struck up bright merry tunes which showed no signs of ever coming to an end. "What is that infernal music, Julius?" asked the surgeon. "Russian folk music, I believe," was the reply. "Can't you get the band to play something soothing—Strauss or Lehar?" suggested the tired traveller, and his host approached the orchestra. "But your friend, he is not Russian?" inquired the excited Kapellmeister. "No," came the firm reply, "he is English." "Then ve must play, *It's a long long vay to Tipperary*."—It certainly was.

* * *

A surgeon must face many risks. But there is one in Africa which no insurance policy covers. Here is what happened. An African was brought to hospital with an acute abdomen. He was operated on. There was a perforated appendix and generalised peritonitis. He died. His relatives and friends then went on strike. They said: "The doctor is a great magician. He can, if he wishes, make our brother live again. But perhaps his magic is not strong enough. Then he must marry the widows of our dead brother. We shall agree to his taking over the children, among whom are some girls, who will bring him many oxen one day when they are marriageable." It was pointed out to them that the offer of the children going with the widows was appreciated, but wasn't their offer unfair to the brothers and nephews of the deceased, who, by native law, inherit the widows and children? That shook them a bit. In the end a payment of £25 settled the matter.

* * *

Colin's mother is perturbed over his asthma, since he caught it in such unauthorised fashion. His school friend comes of a sporting family who keep racing greyhounds. One evening at play, when they were seven years old, the friend brought out to share with Colin two boxes of the dogs' special racing tablets. ("The label says: *To give to soldiers, sailors, and airmen when all hope is abandoned*, doctor.") Highly strung as he was by nature, Colin by the end of his second tablet was keyed up to blow the roof off. His family spent a restless and unhappy night with scant benefit of bromide. "And ever since the tablets he's had this asthma come on him."

* * *

Cross my heart, this is an exact copy of a letter received by a clinic nurse in my district.

Dear Miss the Nusse

You sent Harry home becos he smeld. He just smeld as his father did an Ive slep with him 20 yrs an he soots me very well so you will have to make him soot you.

Mrs. . . .

Letters to the Editor

M.R.C.P. EXAMINATION

SIR,—"Another M.R.C.P." remarked very truly on Sept. 18 that what is wrong with the membership examination just now is "not the system but the excessive number of candidates." He makes three good practical suggestions for deterring "sportsmen from putting a bit on the membership as if it were a horse"; but, like other correspondents, he does not inquire into the reason for this recent embarrassing increase in the number of young medical sportsmen. No doubt there is more than one cause or motive, but I am quite sure the increase derives mainly not from an outburst of sportsmanship, a sudden lust for learning, or desire for a crown of wild olive, but from the flight from general practice, easily predictable at the time of the white-paper and now plainly visible to all not wilfully blind.

The young man sees, looming close ahead, a statutory definition of consultants and specialists which, for physicians, will include the membership. He sees the existing ditch which splits the practising profession being industriously deepened and widened, its banks heightened and concreted, the bridges over it destroyed and no new ones built or even planned. Beyond it he discerns the Accredited Consultants, to whom shall belong whatever of honour, glory, power, and dominion the profession may enjoy, substantial salaries, at least some freedom to define their own fields of activity, that protection from exploitation which belongs to institutional practice, and at least some proportion between reward—financial or other—and quality of work. On his side he sees "the rest," general practitioners rather by inference than definition, the Universal Providers, the indispensable but unhonoured middlemen, the unlockers (on request) of the medical toy and sweet cupboards, defenceless against exploitation from below or regulation from above, shut out from the hospitals and unsupplied with ancillary services, remunerated quite without regard to quality of work, qualifications or proved ability. This is the "set-up" for the future the young man sees, accepted by Parliament, disliked but not rejected by his profession, seemingly intended to be permanent. I suggest that unless widening operations on the dividing ditch are called off, bridges constructed without delay, and conditions of professional life and rewards for good work on the near side brought up to those on the far, the pressure of unlikely candidates on the membership and fellowship examinations will be the least of the evils we may expect to fall on medicine, on our profession, and, of course, on the public, who still do not understand that what is bad for medicine and the profession must be bad for them.

London, N.W.3. LINDSEY W. BATTEN.

INFANTILE GASTRO-ENTERITIS TREATED WITH STREPTOMYCIN BY MOUTH

SIR,—It is encouraging that Dr. James and her colleagues (Oct. 9, p. 555) have found streptomycin to be an effective drug in the treatment of infantile gastro-enteritis, but it is profoundly disappointing that they have not reported an effectively controlled experiment on a large number of cases. Gastro-enteritis, of all conditions, is one in which the severity and the mortality varies in different individuals, different countries, towns, and hospitals, and in the same hospital in different years, so that in one epidemic no deaths may ensue while in another a third or more of the affected babies may die.

This paper reports the results with streptomycin in three groups of cases. In group A, 4 newborn infants received the drug and are compared with 23 cases treated by "routine measures." There were no deaths and it is claimed that following streptomycin the 4 treated cases, though "the most severe in the outbreak," recovered more rapidly than the 23 untreated. In group B—12 infants in a residential nursery—4 cases, including 3 which were "much more severely ill than any of the controls," received streptomycin some days after diarrhœa had commenced, while 8 had no streptomycin. Again there were no deaths and again it is claimed that response to streptomycin was rapid. The way in which the authors

Digitized by Google

have assessed response to treatment is difficult to follow since it is not clear precisely how weight increases have been reckoned. Moreover, as is admitted in the statistical analysis, the two groups A and B are not strictly speaking controlled experiments. Is it possible to subject the results on so few cases in a disease so variable in its course and outcome to such a detailed statistical analysis?

Finally, in group C, 30 cases were given streptomycin without controls of any kind and it is claimed that they recovered surprisingly rapidly. For instance, "the speed of their response to streptomycin therapy was spectacular" in 3 cases, 2 cases "responded well to streptomycin," and more generally "It is probable that, if cases were treated with streptomycin at the onset of gastro-enteritis, starvation could be safely omitted and generous feeds given throughout the illness." This may all be true, and if it is then streptomycin will save more lives and in much smaller doses than it will ever do for tuberculous meningitis. But surely we can expect to be given more substantial evidence of the beneficial results of a new drug in the treatment of a common and dangerous disease before being encouraged in such a sweeping way to apply it indiscriminately. For that, we submit, will be the result of this paper.

Our own results, based on some fifteen months' experience of streptomycin in gastro-enteritis in the East End of London, now being collected for publication, not only confirm the findings of Dr. James and Mr. Kramer that the gut is rapidly cleared of such organisms as *Proteus vulgaris* and *P. morganii* but also indicate that these organisms rapidly reappear within a few days of withholding the drug. They suggest, moreover, that their presence, their coming and going, or their absence have little bearing on the ætiology of the disease. But we have not, unfortunately, been able to demonstrate by controlled alternately treated cases that streptomycin materially affects the course or prognosis of the disease.

This letter is written in the hope that before streptomycin is made free for general use in gastro-enteritis more convincing evidence of its efficacy will be forthcoming.

IAN M. ANDERSON
RICHARD H. DOBBS
B. LEVIN
B. MCNICHOLL.

Gastro-enteritis Unit.
Queen Elizabeth Hospital
for Children, London.

TRANSVERSE MYELITIS COMPLICATING PNEUMONIA

SIR,—Dr. Suchett-Kaye's report in your issue of Sept. 11 recalls a very similar case in this unit.

The patient, a young man of 18 in the Royal Air Force, was admitted to hospital on Nov. 7, 1947, complaining of pain in the right side of the chest. On admission his temperature was 103°F; there was a patchy erythematous rash over the face and chest, and some exudate over one tonsil. Administration of 'Sulphamezathine' was begun, and the next day he developed a cough with sputum, and increased pain in the chest aggravated by deep breathing. At this time signs of a right pleural effusion appeared, and turbid yellow fluid containing large numbers of lymphocytes was aspirated. X-ray examination of the chest revealed patchy consolidation of the right lower and middle lobes.

On the 6th day of his illness he complained of pins and needles in his legs, and by the 8th day he had a complete flaccid paraplegia with loss of all sensations below the level of the 10th dorsal segment. Lumbar puncture carried out at that time revealed a block in the spinal pathways, as evidenced by yellow fluid with a protein content of 500 mg. per 100 ml. and no response in the manometric reading following jugular compression.

He was transferred to this unit and lumbar puncture 2 days later revealed free pathways and a clear fluid. On admission he was put on heavy doses of penicillin. His right pleural cavity was aspirated on two further occasions. On the first of these a little thick pus was obtained from which a pure culture of *Staphylococcus aureus* was grown. On the second occasion there was a little turbid fluid only, which was sterile on culture.

The patient's chest condition resolved, but the paraplegia remained complete and he developed large septic pressure-sores and a urinary infection which brought about his death on April 10 this year. Autopsy revealed typical transverse myelitis of the cord with organised adhesions in the right chest over the lower lobe.

ARNOLD S. ALDIS
Senior Assistant in the Surgical Unit,
Welsh National School of Medicine.

Royal Infirmary,
Cardiff.

PROPRIETARY MEDICINES UNDER THE NATIONAL HEALTH SERVICE ACT

SIR,—My article of Sept. 18 (p. 465) was essentially concerned with the professional use, under the Act, of "ethical" proprietary preparations, but as Dr. Forster's letter of Oct. 9 introduces some wider questions I will try to answer these under general headings.

Definition.—Two types of proprietary medicines are generally recognised: (1) "ethical" preparations, sold mainly on doctor's prescriptions, orders, and recommendations, and not advertised to the lay public; and (2) preparations suitable for use without medical supervision, which can be described as "domestic" proprietaries. (These two types are identified by the Chemists Federation as "class A" and "class B" products.)

Uses, Including N.H.I. Prescribing.—Dr. Forster is correct in saying that the more dramatic advances (as ethical proprietaries) were accepted under N.H.I., but his examples did not indicate the general attitude of the Ministry to these preparations. My article contained data (apparently ignored by Dr. Forster) which provided reasonable proof that the methods used to check excessive prescribing resulted in a loss of professional freedom and responsibility.

Domestic proprietaries often provide a useful means of treating minor ailments, and to bring every minor disorder under medical control would seriously embarrass both the medical profession and the Minister.

Methods of Control.—The Medicine and Pharmacy Act, 1941, the Food and Drugs Acts, and the Labelling of Foods Order, 1946 (and amending Orders), require the disclosure of the composition of proprietaries, but there are no criteria for the official or non-official recognition of ethical proprietary medicines such as the approved list of the American Council on Pharmacy and Chemistry. My suggestion was an advisory body to the Minister to provide expert interpretation, when required, of the criterion "significant therapeutic advantage" (over existing *B.P.* preparations). Dr. Forster and I at least agree on the principle of a separate body.

Domestic proprietaries are controlled (1) in respect of composition, as detailed above; (2) by statutory restrictions prohibiting the non-medical treatment of certain diseases specified in the Venereal Diseases Act, 1917, the Cancer Act, 1939, and the Pharmacy and Medicines Act, 1941; (3) in part by the standards which have been set up by such bodies as the Chemists Federation, advertising associations, and others.

The Chemists Federation has been mainly concerned with domestic proprietaries, but I must correct Dr. Forster's assumption that the federation's purpose is merely to promote the sale of proprietary preparations. There are two kinds of monopoly—that which is justified by serving the public interest and that which is not. The monopoly which the federation attempts to establish for pharmacists in respect of the distribution of proprietary medicines finds its justification in the specialised knowledge of the pharmacist and the standards laid down by the C.F. Standards Committee [1]—probably the most significant contribution yet made towards the elimination of abuses attending the sale of this class of proprietary preparation. I must also question Dr. Forster's statement that the federation cannot completely serve two masters—the medical profession and the trade. Doctors are not directly interested in the domestic proprietary, but I am sure Dr. Forster will agree that if both doctors and the pharmaceutical industry are serving the public welfare there will be no fundamental diversity of interests.

Pharmacy.—Dr. Forster has not, I think, taken into account the many highly specialised techniques and

1. *Work of the Standards Committee.* Obtainable from the secretary, Chemists Federation, 4/5, Queen Square, London, W.C.1.

Digitized by Google

large-scale processes used in the production of pharmaceuticals which have made it impossible for the pharmacist to dispense, extemporaneously, all the preparations which modern research has placed at the doctor's disposal. This, of course, applies to the ethical proprietary. With the domestic proprietary the work of the Chemists' Federation has made it possible to envisage the integration of all the pharmacist's activities, since his professional interest in, and understanding of all C.F. proprietary preparations has been justified.

Suggested Principles in Evolving Controls.—Since voluntary control is far healthier and far less expensive, both in money and personnel, than statutory controls, the latter should be kept to a minimum. To encourage progress and enterprise the State should be prepared to offer appropriate rewards. Is not the inclusion of the list of substituted proprietary preparations in the *N.(W).F.* directly opposed to such a principle? The medical practitioner should be free to prescribe what he judges to be medically necessary for his patient, so that the initial responsibility for deciding what drugs are necessary is placed where it rightly belongs—in the doctor's hands. This principle has been subscribed to by the Minister, though it remains to be seen how far it will be applied to proprietary medicines.

The medical profession has been well, and often brilliantly, served by the pharmaceutical industry—a contribution to the health and prosperity of the nation which a narrow or shortsighted policy can destroy.

London, N.W.10. E. W. GODDING.

MEDICAL SECRETARIES

SIR,—May a woman have the last word on this subject? As a medical secretary myself, I should like to uphold the claim for special training of medical clerical workers. If I had wanted to take up nursing, physiotherapy, social service, or any other work connected with a hospital, I should certainly not have been accepted without suitable preliminary training; yet I came into my job from one of the Services (and before that a commercial office) with the haziest knowledge of medical terms and hospital procedure. For the first week or two I was in despair, and probably the medical staff weren't too happy either. Having, fortunately, a good memory for words, I worried through and now wouldn't change my job for anything. But every day makes me realise what a lot of technical words I *don't* know, and I should welcome a training course which would give me something of the general groundwork of a nurse's training.

Medical secretaries believe that their status would be raised if inducements were offered to young girls to make this a career. With my seniors, housemen, and consultants to type for, and my clinics, waiting-lists, card indexes, two telephones, and other time-occupiers, I don't feel I work any less hard than my colleagues in the technical sections; and I should like to feel that I will eventually reach their rate of pay and length of holidays. Bearing in mind the number of hospitals and doctors needing clerical help, is it too much to ask for specialised training for youngsters who would "love to work for a doctor," but get panicky if asked to spell "appendicitis"?

DOCTORS' SECRETARY.

ANOMALY OF ABDOMINAL MUSCULATURE

SIR,—An unusual anatomical anomaly was found in a man who lately came to me for removal of a vesical pouch.

The patient was aged 69. The abdominal wall was apparently healthy, and the bladder, which had a pouch the size of a billiards ball, was approached by a transverse incision through the aponeurosis overlying the rectus. Instead of the vertical disposition of the muscle beneath the sheath, I found subjacent fleshy fibres passing horizontally to the linea alba. Although momentarily stunned by this, to me, unique anomaly, I quickly realised that, instead of becoming aponeurotic at the linea semilunaris, the flesh of the internal oblique had continued over the face of the rectus abdominis. The right rectus appeared average, but the left some 40% sub-average.

This variant had apparently not impaired the efficiency of the parietes. The wound healed normally.

Bristol. A. WILFRID ADAMS.

UNDER TENSION

SIR,—Among all the sorts that read THE LANCET there will be those who disapproved of your leader of Oct. 9, and those who approved of it. I should regret that only the former should be represented in your correspondence columns. To others of us your sober reflections round the theme that "it takes all sorts to make a world" contain something more than a half-truth when we are faced with Dr. Chapman's alternative—to look at one half of the world as one who "repeatedly attempts to destroy him and who proclaims, fortissimo, his intention of going on trying . . . ." We seem to glimmer Dr. Chapman's logical counter to that one.

We are clearly enough in a dangerous situation. Dr. Chapman has heard voices and he isn't the only one. Are those voices real? Are they by any chance also heard in Russia? There is always something of fact for international paranoia to batten on. But how little relative to the issues of sane settlement! And, taking the long view (say 40 years in this case), how fundamentally equal are the intolerances and the provocations of the opposing sides! Are threats to vital interests (implied or felt) ever limited to one side in a major international dispute?

It may one day become clearer that the threat which 1948 offered to our world was not primarily that the policy of any power-group aimed at the destruction of the vital interests of any other power-group, but that everywhere people *came to think this so*. Some individuals and some peoples may have more of suspicion to unlearn than others; some undoubtedly have more to unlearn of cruelty to their foes. But shall that thwart our peaceful solution? Such complaints are perennial. Grotius, a Dutchman, tried to set up international law in 1625 but decided that one couldn't cope with the Portuguese.

What we lack is scientific machinery for settling international disputes despite the froth of irresponsible journalism and the honest prejudice of so many men and women. What more appropriate, then, to THE LANCET's last than that it should chase the mental health of peoples a little further than did our recent international congress by reminding us where we stand today? To secure world order, international legal machinery has to be made just as calm, dispassionate, and secure as our own domestic courts of law—simply because it takes all sorts to make a world and (may I add?), because to err is human.

Edinburgh. RANYARD WEST.

HOW MANY NURSES?

SIR,—Dr. Cohen takes as the criterion of nursing and medical effectiveness in hospital the patient's duration of stay "which is assumed to be an index of his duration of sickness." *Is* this assumed by anyone who stops to examine and consider the factors governing admissions to and discharges from hospital?

It is possible that duration of sickness might be accepted as one criterion (among several) of effective care, but it is surely very dangerous to single out that chapter in any individual's ill health which he is allowed or persuaded to spend in hospital, and which may occur at an early or a late stage of his illness, as the index of the duration of sickness. One hopes that at present the hospitals, hard-pressed though they are by waiting-lists, take into consideration the home circumstances of the patients before deciding at what stage of invalidism or of recovery they may safely be allowed to leave. I know that this is an important factor to the good ward sister, whether surgical, medical, or obstetric. To take the simplest instance, has the anxious primipara sent out on the 8th day to a comfortless home (where she immediately "loses her milk" and learns by failure) really received more effective care than the one who goes out on the 14th day or later with a little additional confidence, stability, and knowledge of her new responsibilities? The same applies in the fields of surgery and of medicine. It may be expedient sometimes to shorten duration of stay in the interests of the total sick population, but we need not pretend that it means better nursing or medical care for the individual.

One hates to think that a hospital might be led by Dr. Cohen's hypothesis to make quick turnover of

Digitized by Google

patients its criterion of efficiency. Perhaps such a hospital would experience a rise in the number of relapsed patients who had to be readmitted; unless, indeed, they took their troubles to other institutions where results were measured in terms of health and comfort and not in numbers.

If we had to live in a house which a jerry-builder had run up on inadequate foundations in a few weeks, we should not esteem him the better workman merely because he turned out houses faster than one who built well and truly. The implications of this are infinitely more important in the building up of health and happiness.

MURIEL M. EDWARDS
Secretary,
Nursing Recruitment Service,
King Edward's Hospital Fund.

21, Cavendish Square, W.1.

ABORTION, STERILISATION, AND THE LAW

SIR,—The following case seems to me to be of sufficient general interest to merit discussion in your journal, and to show the necessity for a change in the present laws concerning abortion and sterilisation.

Miss X.Y., aged 31, was brought to me by her mother, with a request that I should terminate the pregnancy and sterilise the patient. She had been referred to me by two specialists in psychiatry, to one of whom she had been referred originally by her own family doctor.

The family doctor certified as follows: "I have known Miss X.Y. for ten years. She is mentally deficient and unstable and is now pregnant by an unknown man. I consider that the pregnancy should not be allowed to continue, and, as the same thing may occur again owing to her disposition, that she should be sterilised." This letter was accompanied by a letter from the rector of her village, who said: "I have known Miss X.Y. for the past ten years and have had close contact with her family for the same length of time. She is, in my opinion, unbalanced mentally, and completely unfit mentally to be responsible for the care and upbringing of a child."

Psychiatrist no. 1 certified: "I consider this patient quite unfit to proceed with her pregnancy on account of her psychiatric condition. She is mentally and emotionally unfitted for motherhood on account of her limited intelligence and emotional development. This is, in my opinion, a clear case for the termination of pregnancy and sterilisation." The second psychiatrist wrote: "The patient is very limited in intelligence and is emotionally unstable. She would be unable to look after a baby and is likely to harm it during a temper outburst. I recommend termination of pregnancy and sterilisation."

After interviewing the girl myself, I had no hesitation in agreeing that it was clearly desirable, in the girl's own interest and in the interests of the community, that the pregnancy should be interrupted, and that she should be rendered incapable of becoming pregnant in the future. But, remembering the famous case of the American millionaire's daughter who, some ten or twelve years ago, took action against her mother, who had had her sterilised, and against the doctor who had performed the operation, I wanted to make quite sure that I was not rendering myself liable either to a criminal charge, or to a civil action.

I therefore sought the advice of the Medical Defence Union, the secretary of which pointed out that none of the other three doctors or myself had certified that the continuation of the pregnancy would endanger the life, or the mental or physical health, of the mother herself, and that therefore there was no legal ground for terminating the pregnancy. He also pointed out that it was not clear whether the patient was, or was not, really capable of giving valid consent, either to termination or to sterilisation.

After exhaustive discussion, we decided, very reluctantly, that we could not safely perform either operation.

The Act forbidding abortion is far from clear. It forbids "wrongful" termination of pregnancy, without defining the meaning of the word wrongful. The interpretation generally accepted is that it is wrongful unless the continuation of the pregnancy seriously endangers the life or health of the mother. And none of us has the courage to terminate a pregnancy in a case like the present one, and so run the risk of imprisonment and loss of the right to earn our livelihood by the practice of our profession. Nevertheless, I cannot believe that any court would find a surgeon guilty if he were to terminate the pregnancy in such a case, supported, as it is, by the opinions of the patient's own usual medical attendant, her spiritual adviser, and two psychiatrists of standing.

With regard to sterilisation, the law is equally vague. Some medicolegal authorities are of opinion that sterilisation of a man or woman, sane and adult, with the patient's consent, could be regarded as *mayhem*, but, according to the *Encyclopædia Britannica*, mayhem signifies an assault "whereby the injured person is deprived of a member proper for his defence in fight, e.g., an arm, a leg, a fore tooth, etc. The loss of an ear, jaw tooth, etc., was not mayhem." I do not see how sterilisation, carried out by cutting and tying the sperm-ducts in the male, or the fallopian tubes in the female, could possibly be interpreted as mayhem, and I believe that the voluntary sterilisation of a sane adult is not forbidden by English law.

But an insane or mentally defective person is rendered incapable, by the very fact of insanity or mental deficiency, of giving valid consent; so, in the very cases where sterilisation is most desirable, it is not permitted.

Is it not time that the profession should move for the alteration of the laws relating to both abortion and sterilisation?

NORMAN HAIRE
President, Sex Education Society.

London, W.1.

TESTS FOR THIOURACIL SENSITIVITY

SIR,—There is no known régime which will guarantee freedom from toxic complications, including neutropenia, during thiouracil therapy. Hence a simple method of differentiating susceptible and non-susceptible people would be of great value.

It occurred to one of us (E. K. B.) that skin tests in association with serial leucocyte counts might fulfil this function. After consultation with Messrs. Genatosan Ltd., Mr. H. J. Benzies, chief pharmacist at the Royal Infirmary, Sheffield, prepared sterile solutions of methyl thiouracil (1/2000) and of propyl thiouracil (1/1000) in distilled water. Sterilisation was effected by steaming for 30 min. The preparations were put up in rubber-capped bottles and kept in the refrigerator when not in use, no preservative being added. Crystals occasionally separated out in the cold, the above-mentioned concentrations being near saturation level in each case. However, the crystals redissolved when the bottle was placed in warm water for about a minute.

The subjects for the tests were divided into the following groups:

(1) Non-thyrotoxic persons, 18.

(2) Untreated thyrotoxic patients, 3.

(3) Thyrotoxic patients treated with methyl or propyl thiouracil who had shown no toxic reactions, 6.

(4) Thyrotoxic patients treated with methyl or propyl thiouracil who had previously developed toxic manifestations, 4.

Throughout the tests the subject rested quietly in bed or in a chair, no food or drink being taken, and smoking not being allowed.

Each person was submitted to two tests:

(1) Into one forearm 0·1 ml. of 1/2000 methyl, or 1/1000 propyl, thiouracil was injected intradermally and a similar amount of sterile distilled water was injected intradermally into the other forearm as a control. Treated patients were injected with the type of thiouracil that had been given during treatment.

(2) As in (1), except that the injections were given subcutaneously.

Readings were made after 5, 20, 40, and 60 min., and 24 and 72 hours.

These tests gave completely negative results, with two exceptions:

(1) Mrs. A developed a light-brown pigmentation at the site of the intradermal methyl-thiouracil injection, after 72 hours. This gradually faded in the next few days. The patient had previously had agranulocytosis accompanied by a generalised erythema, following treatment with methyl thiouracil.

Digitized by Google

(2) Mr. B, who had had a severe but symptomless methyl-thiouracil neutropenia, showed an exactly similar pigmentation.

In 8 of the cases (3 non-thyrotoxic, 1 thyrotoxic treated with methyl thiouracil who had shown no toxic symptoms, and 4 thyrotoxic treated with methyl or propyl thiouracil who had shown toxic reactions) tests were performed as described above but, in addition, were repeated with sterile distilled water instead of methyl or propyl thiouracil for all injections. They were read at the same intervals as before and were all negative.

The fact that, in the cases investigated, skin tests alone were of no value is not surprising. In general, skin reactions are not constant or reliable in alimentary allergy.[1] With the exception of true eczematous and, occasionally, true urticarial eruptions, it is generally impossible to predict by skin tests whether a person will or will not show hypersensitivity to a given drug. Nor do responses to skin tests indicate the type of clinical reaction which may develop.[2]

In the 8 above-mentioned cases total and differential leucocyte counts were made before each of the four tests and at the time of each reading thereafter. One further test was performed on these patients—leucocyte counts were made at the same intervals after an arbitrary fixed time, no injection having been given.

The number of cases in this series is far too small for generalisation, but test no. 1 showed that the total leucocyte and absolute granulocyte counts fell more precipitously in the thyrotoxic patients who had previously shown toxic reactions (leucopenia and neutropenia) than in either the controls or the single thyrotoxic patient on methyl thiouracil who had not previously shown toxic manifestations.

Further work is being done to confirm or refute our original impressions.

We are indebted to Prof. E. J. Wayne and Dr. H. P. Brody for access to their cases; and to Mr. H. J. Benzies and his staff, and Dr. D. Hobson, for their help and technical assistance.

E. K. BLACKBURN
J. F. GOODWIN
R. H. CANTER.

Sheffield.

COMPULSORY ADMISSION

SIR,—This morning I was compelled to go to the rescue of one of the casualty officers of my hospital, who had been ordered to admit a chronic patient to a non-existent bed by an individual, apparently a doctor, stated to be speaking on behalf of the Emergency Bed Service. If this is a foretaste of official policy, I feel its implications should be clearly understood. A few years ago the world was shocked by revelations of the workings of an institution run on a comparable principle. Though I am not concerned to defend the official who was in charge of that institution, there was justice in his contention that, as he had no control over admissions and his protests to central bureaucracy were ignored, he was not responsible for the overcrowding and neglect within his walls. His name was Kramer and his institution was at Belsen. Let us not build the like for the chronic sick of England.

X.Y.

*** Since July 5, the Emergency Bed Service of the King's Fund has continued to assist doctors who ask for its help with the admission of urgent cases to hospitals in London. The E.B.S. has no power to compel any hospital to admit a patient. On the other hand, a doctor has been appointed to represent the Metropolitan regional hospital boards at the E.B.S., so that when no vacant bed can be found for an urgent case he may call on the appropriate hospital to make special arrangements for the patient's admission. It seems to us that the boards must retain the right to do this, though in present circumstances the right should be very sparingly exercised. We should be interested to hear more about this "chronic patient."—ED.L.

1. Dameshek, W., Colmes, A. *J. clin. Invest.* 1936, **15**, 85. Holten, C. *Amer. J. med. Sci.* 1937, **194**, 229.
2. 1945 Year Book of Dermatology and Syphilology. Chicago; p. 27.

REGIONAL SPECIALIST COMMITTEES

SIR,—It is only six months to the end of next March, and many regions have not yet formed a representative regional specialist committee which can be certain that its delegates to the central committee really speak for the region as a whole.

In the Liverpool region we have two associations, the Hospital Staffs Association and the Regional Hospitals Medical Association, that between them cover the majority of the specialists working in the region. These two bodies have sponsored a suggestion that the Liverpool Regional Specialists Committee be reconstituted with representatives nominated as follows:

2 by the Liverpool University faculty of medicine.
8 by the Hospital Staffs Association for the teaching hospitals.
8 by the Liverpool Regional Hospitals Medical Association for the regional board hospitals.
2 by the north-western branch of the Medical Superintendents Society.
2 by the registrars, 1 to be from the teaching hospital group and 1 from the regional hospital group.
1 from the Isle of Man.

This will give a completely representative committee, and we believe that all sections will feel satisfied. We hope that any above the rank of house officer who are not already members of the Regional Hospitals Medical Association, if employed in a regional board hospital, will join us.

We are most anxious that the old difference between voluntary and municipal hospitals should not reappear in a different guise in those now set up, and we welcome the coöperation that we have received from the Hospital Staffs Association.

V. COTTON CORNWALL
Hon. Secretary, Liverpool Regional Hospitals Medical Association.

The Poplars, Lower Lane, Liverpool, 9.

THE YOUNG CONSULTANT

SIR,—It is interesting and an occasion for sympathy to read in your leading article of Oct. 16 of the meagre amount paid to general practitioners in the first quarter of the National Health Service. But the plight of the junior consultant is considerably worse than that of the general practitioner. Having spent double the time learning his job, and a not inconsiderable sum on instruments, consulting-room, and a dwelling-place, the young consultant finds that private practice has practically vanished. Conversely, hospital work has increased and a considerable amount of time and petrol has been consumed since July 5 in journeys to cottage hospitals and on domiciliary visits, to say nothing of telephone calls, stationery, and the like. The only acknowledgment of claims for payment so far received is a reference to certain domiciliary visits which are apparently not allowed for payment!

Incidentally, a promised interim payment of the staff of my hospital is still owed from July, 1947. It would be interesting to see what would be the result if sections of the so-called working class were kept waiting for fifteen months for their wages.

JUNIOR PROVINCIAL CONSULTANT.

MEDICAL RECORDS

SIR,—As a medical student, and later as a junior resident, one had the impression that potential ability was largely assessed by the accuracy and completeness of one's case-notes. Slovenly notes implied a slovenly student or house-physician, and such records used to be torn to shreds verbally and actually before an awe-struck assembly of clerks or dressers. This attitude of the chief was surely correct. Complete records can only proceed from a complete anamnesis and examination—the twin foundations of medical craftsmanship.

It would perhaps be too harsh a generalisation to translate this thesis into broader terms and state that the work of a hospital may be appraised by its clinical records, yet it is quite certain that no hospital can fulfil its purposes to best effect when encumbered by archaic methods of record-keeping. The truth of this is apparent to anyone who has experienced the contrast of work in hospitals well served and badly served in this respect.

Digitized by Google

The report of the King Edward's Hospital Fund [1] will therefore be welcomed by clinicians working in hospitals where the term "records officer" is as yet meaningless. Throughout the country the advent of the National Health Service must have tended to freeze administrative initiative, and on the subject of medical records the Ministry has offered no advice. In this, as in so many other matters worthy of prompt attention, "awful darkness and silence reign over the great Gromboolian plain." Let us hope that the report may be followed by an efficient and nation-wide directive to hospital management committees, laying down the broad principles along which record departments should be planned, but leaving the initiative of reorganisation at the periphery.

Wolverhampton. J. V. S. A. DAVIES.

DENTURES AND ANÆSTHESIA

SIR,—From the Dark Ages nurses have been taught to remove the patient's dentures before the administration of an anæsthetic. The edentulous patient is left with sunken cheeks and loose, floppy, flapping lips. The sunken cheeks prevent a close fit of mask to face. The flapping lips obstruct the airway. In laryngoscopy for intubation, the laryngoscope may cut the gum and slip from side to side. If the denture be left in place laryngoscopy is more easily accomplished, and the teeth can be protected by a piece of strapping. For the past ten years I have made a practice of leaving all *full* dentures in position, without accident of any kind.

Last, but not least, some lady patients suffer intense distress when appearing in the theatre as "toothless old hags," as one poor victim put it. There can be no risk in leaving a full set in position so long as the anæsthetist knows they are there. He is no anæsthetist if he has not looked.

Carshalton. H. PARRY-PRICE.

Obituary

JOHN WILLIAM SCOTT MACFIE

M.A. CAMB., M.B., D.SC. EDIN., D.T.M.

WE have to record the death at St. Leonards on Oct. 11 of Dr. J. W. S. Macfie, a worker of eminence and erudition in many branches of tropical medicine. Born in 1879, he was educated at Oundle, at Cambridge, and at Edinburgh, where he graduated in medicine in 1906. After working in various laboratories, including the physiology laboratory at Liverpool under Sherrington, his interests turned to tropical medicine. He took the diploma in tropical medicine at Liverpool in 1910 and then went to West Africa, where he served on the medical staff from 1910 to 1923 and was director of the Medical Research Institute at Accra from 1914 onwards. During this time he contributed much to knowledge by his work on a variety of tropical diseases, especially trypanosomiasis and malaria. In 1917 he was seconded to the Liverpool School of Tropical Medicine to undertake special research on malaria, and in 1919 he was awarded the school's Mary Kingsley medal for distinguished achievement in the field of tropical medicine.

On retiring from West Africa Macfie joined the staff of the Liverpool School of Tropical Medicine as lecturer in protozoology, and later he worked on the chemotherapy of malaria, under the ægis of the Medical Research Council, at the London School of Hygiene and Tropical Medicine. In 1935, despite failing health, he went to Ethiopia as a member of the British Red Cross unit serving in that country; a record of those experiences was subsequently published in *An Ethiopian Diary*. In 1941, on his insistent request, he was appointed to the Royal Army Medical Corps for overseas duty, and he served with distinction in nos. 3 and 8 malaria field laboratories in Egypt and in the Middle East as a malariologist until a breakdown in health in 1943 obliged him to return to this country. Here he renewed his old interest in taxonomic studies at the British Museum; and he went back for a short time to the Liverpool School of Tropical Medicine, where he was engaged in preparing an instructional film on malaria.

1. Some Observations on Hospital Admissions and Records. London, 1948. See *Lancet*, Oct. 9, p. 578.

Macfie was a world authority on the midges (Ceratopogonidæ), and was largely responsible for the identification and classification of the collection of these insects in the British Museum. Tall and ascetic, he had a kindliness and an unassuming mien that endeared him equally to his contemporaries and to his junior colleagues, many of whom recall with gratitude his unostentatious benefactions.

CHARLES EDWARD LACEY

M.B. LEEDS, D.P.M.

Dr. C. E. Lacey died on Oct. 3 at the age of 29 at the National Hospital, Queen Square, where he was registrar of the psychiatric department. A Yorkshireman, he was educated at Knaresborough Grammar School and at Leeds University, where, after earning many distinctions and scholarships, he graduated in 1942. Six months later he joined the Army, in which he served till 1945, and as section officer of a parachute field ambulance he took part in the invasion of Europe. After a year's training in general medicine in Leeds and Bradford he was awarded a fellowship in psychiatry at Crichton Royal, Dumfries.

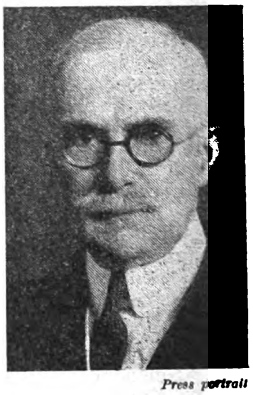
W. M.-G. writes: "Strict and critical with himself, kind and cheerful with others, Lacey was imbued with an ardent love of life. His keen and penetrating mind, his quick grasp of essentials, and his natural gift as a physician gave legitimate hope that a useful career lay before him as a specialist of academic standing. Certainly psychiatry can ill afford to lose a young man of his ability and character."

Dr. Lacey married Dr. Gaynor Jones, who is also a psychiatrist.

HARRY EDWIN BRUCE BRUCE-PORTER

K.B.E., C.M.G., M.D. BRUX., M.R.C.S.

Sir Bruce Bruce-Porter, who died at his daughter's home in Somerset on Oct. 15 at the age of 79, will be widely remembered for his forceful but kindly personality, his zeal in many good causes, and his ability to gain public attention for them. He was born at Woolwich, the son of Captain J. Porter, R.A. At the London Hospital he won scholarships in anatomy, physiology, and clinical medicine, and also the Duckworth Nelson scholarship in practical medicine and surgery. He qualified in 1892, and two years later, after postgraduate study in Brussels and Vienna, obtained his M.D. Brux. with distinction. At the Army Medical School at Netley in 1893 he obtained honourable mention in military medicine, clinical medicine, and surgery. After holding a commission as surgeon captain on the Army medical staff he returned to civilian practice, but he retained his connexions with his old service both as a Territorial and as physician to the King Edward VII Hospital for Officers. When war broke out in 1914 he held the rank of lieut.-colonel and was placed in administrative charge of the 3rd London General Hospital at Wandsworth. In this hospital, which ultimately had 2600 beds, many Dominion troops were cared for, including 20,000 Australians. In 1916 he commanded the 40th British General Hospital in Mesopotamia. For many years he was a military member of the council of the Territorial Force Association in London.



Press portrait

Bruce-Porter's military background made natural the devotion he gave to the work of the St. John Ambulance Association and the Red Cross, of whose joint council he was formerly a member. A knight of grace of the Order of St. John of Jerusalem in England, he was a member of the order's general chapter. But his work for charity was many-sided: he helped to secure recognition for blind masseurs, he was vice-president of the Shaftesbury Society and Ragged School Union, and he gave special interest to the Bruce Porter Home

Digitized by Google

where children from Dr. Barnardo's Homes can have treatment for bone diseases. His appointments included those of consulting physician to the Murray Convalescent Home, Old Windsor, and medical referee to the Scottish Widows' Fund and other assurance societies, and he served on the Home Office committee which inquired into the working of the Acts for the treatment of inebriates. In the Hunterian society he held office as president.

One of the earlier motorists, he was a founder member of Brooklands, and in his youth he was an enthusiast for alpine sports. He married in 1896 the widow of Dr. J. H. Honeyman, of Auckland, and they had twin daughters. Lady Bruce-Porter died in 1937, and on her death he retired from practice to give even more time to his social work, and to health education. In 1938 he made a world tour during which many of his war-time Service patients were able to welcome him to their own countries. He was appointed C.M.G. in 1917 and created K.B.E. in 1919.

THE LATE DR. WESTERN

Sir Paul Fildes writes: Dr. George Western started his career as an assistant in Prof. William Bulloch's department at the London Hospital at a time when Wright's opsonic teaching was in its early stages. He had collaborated with Bulloch in some early researches and when I first met him in 1906 was in charge of the "inoculation department." This department consisted of Western and only Western. When 28 years later I left the London Hospital "Father" Western was still there in the same small room, imperturbable, reliable, and wise. The "inoculation department" gradually faded out and Western took over most of the contacts with patients, both therapeutic and diagnostic. He made no claim to being a "research-worker" but he became an extremely sound and honest exponent of clinical bacteriology. He had a high degree of technical skill and was probably the first to use venepuncture as a routine clinical method at a time when that sort of laboratory aggression was viewed somewhat askance. By these methods he certainly advanced knowledge of puerperal fever. His nickname sufficiently describes the attitude towards him of his younger contemporaries. He was never assertive but was always there. I was not surprised to hear that during the recent war his sense of duty withdrew him from retirement in the country to a commission in the R.A.M.C.

Births, Marriages, and Deaths

BIRTHS

BEARD.—On Oct. 12, in London, the wife of Dr. Trevor Beard—a son.
CATHIE.—On Oct. 10, at Guildford, the wife of Dr. I. A. B. Cathie—a daughter.
DAVIES.—On Oct. 7, at Cardiff, the wife of Dr. G. R. Davies—a son.
DIXON.—On Oct. 13, at Wigginton, Oxon, the wife of Dr. G. E. Dixon—a son.
HART.—On Oct. 9, in London, the wife of Dr. Philip D'Arcy Hart—a son.
RODGERS.—On Oct. 11, the wife of Dr. T. S. Rodgers—a son.
TAIT.—On Oct. 15, the wife of Dr. A. P. Tait—a son.

MARRIAGES

BELL—USHER.—On Oct. 12, at Richmond, Yorks, Kenelm Digby Bell, surgeon captain, R.N. retd., to Mrs. Constance Usher.
EDDY—WICKENS.—On Oct. 15, at Wimbledon, James Angwin Eddy, B.M., to Margaret Joan Wickens.
OLIVER—ABBEY.—On Oct. 12, in Edinburgh, Michael Oliver, M.B., to Margaret Yool Abbey, M.B.
ROWLATT—WALKER.—On Oct. 2, at Whitley Bay, Basil Rowlatt, M.B., to Sybil Walker.
TWOHIG—MILLER.—On Oct. 14, at Coulsdon, Jeremiah Nicholas Twohig, M.B., to Norah Catherine Miller, M.B.

DEATHS

BRUCE-PORTER.—On Oct. 15, in Somerset, Harry Edwin Bruce Bruce-Porter, K.B.E., C.M.G., M.D. Brux., aged 79.
COLE-BAKER.—On Oct. 14, at Waterlooville, Hants, Lyster Cole-Baker, B.A., M.D. Dubl., aged 83.
LANKESTER.—On Oct. 13, Cecil Pryor Lankester, M.R.C.S.
MACFIE.—On Oct. 11, at St. Leonards, John William Scott Macfie, M.A., M.B., D.SC. Edin., D.T.M., aged 69.
MCVITTIE.—On Oct. 14, at Aldington, Kent, Arthur Craigie McVittie, B.A., M.B. Dubl.
PINCH.—On Oct. 14, at Bideford, Albert Edwin Hayward Pinch, M.D. Brist., F.R.C.S., D.M.R.E., captain, I.M.S. retd., aged 81.
SHEPARD.—On Oct. 15, Arthur Harold Shepard, M.D. Dubl.
SYMES.—On Oct. 11, at Bournemouth, William Legge Symes, M.R.C.S., aged 82.

Notes and News

PROTECTIVE FEARS

As the structure of the mind becomes plainer psychologists are able to generalise and classify. It is perhaps unfortunate that in the babel of medical jargon psychologists speak with a particularly obscure tongue—one that often prejudices or defeats doctors, and is presumably even less comprehensible to the layman. In his book *Conquer Fear*,[1] Mr. John Langdon-Davies sets out plainly what is now known about anxiety, irrational fears, panic states, loss of the sense of reality, and the like, and does it so well that doctors no less than laymen may be glad to read about them. He quotes many letters from the hundreds sent to him when he was writing on this subject in the *People*, and these will be of great help and comfort to people suffering from anxiety states, for they show how common such terrifying symptoms are, and how closely the pattern can repeat itself. This in itself would have been worth doing, for such people suffer a great sense of loneliness and isolation. Since their other great dread is of insanity he has wisely included one letter from a psychotic patient, to show how different are insane beliefs from those associated with anxiety; but he is careful to explain that this condition too can be treated with good hopes of success.

Books like this have been written by psychiatrists and doctors from time to time, though perhaps none with such good understanding of what the patient feels or what kinds of things he is hungry to be told. Mr. Langdon-Davies does more, for he gives some advice—and very sound advice too—on the management of these fear states by those who are suffering them. No doctor need be offended by the way he does it. He explains how impossible it would be to provide adequate psychiatric care for the large numbers affected, and makes it clear, in a tactful way, that many general practitioners simply have not been trained to deal with cases of "fear sickness"; moreover, most of them simply have not the time to do more than exclude serious physical disease and reassure the patient with a stock phrase or two. These people must either do what they can for themselves or go on for years in a crippled state.

He explains simply that these fears have a use for the patient, in that they protect him from some more painful repressed memory. What this may be they are never likely to find out: they must be content to strengthen their position in other ways. He suggests that they should write down their plans in a notebook, setting out the nature of their fears and the occasions on which they arise. Psychosomatic symptoms, once the doctor has explained they are not organic, can be looked at objectively; and depression, fatigue, boredom, and the inability to love can be related to family history and childhood memories. Here for the first time Mr. Langdon-Davies is a little obscure: it is not quite clear what the patient is to do with all the material he uncovers; for though no doubt he will ultimately be relieved merely by remembering and facing it, he will certainly have periods of increased anxiety while he is about it. This is not brought out. One important point is made extremely well, however. Many of these patients feel they are short of love; but their need is not merely, or even chiefly, to receive love but to find somewhere to put the love they have to give. If the family or friends offer no-one who can accept this affection, then it must be placed elsewhere—in socially useful work, if need be. The guilty child who is at the bottom of our irrational fears is sustained and relieved by the knowledge that he is some good to his kind.

The book should be read by relatives as well as patients, for it will make them realise that the patient is ill in the same way as if he had pneumonia or a broken leg; and it contains a good chapter on prophylaxis.

SOCIAL AND PREVENTIVE MEDICINE IN ENGLAND

THOSE who attended Sir Arthur MacNalty's FitzPatrick lectures at the Royal College of Physicians during 1946 and 1947 now have an opportunity to refresh their memory, and those who were not present will enjoy the chance of reading his careful account[2] of *The History of State Medicine in England*. The lectures cover the time from the accession of Queen Victoria in 1837 to the foundation of the Ministry

1. London: Feature Books. 1948. Pp. 173. 5*s*.
2. Published by the Royal Institute of Public Health and Hygiene. 1948. Pp. 82. 12*s*. 6*d*.

Digitized by Google

of Health in 1919; but since preventive medicine, though intimately linked with it, has a much longer history than State medicine, Sir Arthur has included, as an introduction to the volume, his presidential address to the Royal Society of Medicine's section of the history of medicine, in which he reviewed the growth of the preventive idea from the days of ancient Egypt and Greece up to the time of the Industrial Revolution and the great social reformers.

UNION OF ST. LUKE

WE have received the first periodical letter issued by the Union of St. Luke, which was founded this year and has the Bishop of Ely as its president. The union is a professional association of medical practitioners who are communicant members of the Church of England. "It aims to assist such practitioners by means of its fellowship to strengthen their Christian life and witness." The hon. secretary is Dr. R. H. Hardy, 5c, Parkhill Road, London, N.W.3.

CLEANER FOOD

AT their annual conference at Hastings on Oct. 14, the National Council of Women adopted a comprehensive resolution urging the Government to put an end to the loss of food by contamination, by making it compulsory for all local authorities to pass and enforce adequate by-laws for the protection and clean handling of all foodstuffs. The conference, says the *Manchester Guardian* of Oct. 15, also called on the Minister of Health to repeal the exemption clause in section 14 of the Food and Drugs Act, 1938, so that restaurants, inns, &c., would have to be registered in the same way as premises which sell cooked foods over the counter, and demanded a high standard of cleanliness and comfort in trains and railway refreshment rooms and improvement in the standard of food supplied in refreshment rooms.

NECROPSY ON A TRANSFIXIONIST

DETAILS have now been published [1] of the necropsy on Mirin Dajo, who, after surviving transfixion with swords and rods many hundred times, died after swallowing a dagger.[2] Œsophagoscopy revealed that the point of the dagger, which was nearly 14 in. long, had perforated the œsophagus, its blunt head being in the stomach. The dagger was removed by gastrotomy. The wound in the œsophagus healed, and on the seventh day, when the stitches were removed, Dajo seemed well; but about a week later he was found dead. Necropsy showed that local mediastinitis had arisen at the site of perforation and had led to erosion of, and hæmorrhage from, the aorta, which had presumably been scratched by the point of the dagger. Relics of Mirin Dajo's previous multiple transfixions were numerous pleural adhesions (but very few peritoneal adhesions), scars in the liver, and a single scar in the apex of the heart.

AMBULANCE AND FIRE SERVICES

THE Institute of Certified Ambulance Personnel, of which Dr. H. B. W. Morgan, M.P., is president, and Dr. W. W. Fox chairman, was set up to raise the standards of knowledge and service of ambulance personnel and "to minimise the needless pain and suffering which many patients have to undergo when they are transported in ambulances by men whose knowledge, training, and experience is below the standard necessary for their full efficiency." The institute rightly takes its responsibilities seriously, and a recent memorandum by Dr. Fox on the future administration of the ambulance service under the National Health Service Act discusses how far ambulance personnel can usefully be helped in their work by their colleagues, the members of the fire service. Coördination between the two services in the repair and maintenance of vehicles and intertelephonic communications would be welcome as an economy in man-power; but coöperation in the care of the patient is regarded with more reserve. Firemen are trained to deal with the restriction of fire on property and "their whole psychological outlook is one which is associated with destruction; hacking down of timber and using powerful jets." Handling the injured requires a high standard of gentleness and one cannot, Dr. Fox suggests, expect to develop these two qualities in the same person. His memorandum asks readers to consider "what qualifications you would like the individuals to have who would be responsible for your personal transportation."

1. Bessemans, A. *Brux.-méd.* 1948, **28**, 1945.
2. *Lancet*, 1948, **1**, 891.

HOMES FOR THE AGED IN LONDON

LONDON County Council has arranged to purchase four houses for use as small homes for the aged. This is in pursuance of the council's policy, under the National Assistance Act, of establishing such homes in various parts of London wherever they are needed. Each home is to accommodate not more than 80 old people, and the aim is that they shall take considerably fewer. Development of the scheme is likely to be slow, for no new building is to be undertaken, and the amount of money to be devoted to conversion is restricted.

MALARIA CONTROL IN SARDINIA

THE Italian public-health authorities claim great strides in the prevention of malaria in Sardinia (which is about as large as Wales), with the help of the Rockefeller Foundation, by an attack on mosquitoes and their larvæ with D.D.T. and 'Oktaklor.'[1] In 1946 there were 17,000 cases of malaria in the medical district of Cagliari, the southern capital of that island. In 1947 the figure dropped to 6000, of which only 1000 were primary infections, and in the first half of 1948 to 456 cases, of which only 21 were primary infections.

INTERNATIONAL SCIENTIFIC FILM CONGRESS

As mentioned in our last issue this congress, held in London between Oct. 8 and 12, was attended by delegates from 25 countries, who agreed to establish an International Scientific Film Association. Among the matters to be considered by subcommittees are: (1) the establishment of an international data card for compiling a master index of scientific films available throughout the world and the formulation of methods of appraisal of these films; (2) the joint production by a number of countries of films of common interest; (3) the exchange and distribution of scientific films and the customs regulations affecting such exchange; (4) the setting up of a scientific film reference library; and (5) the exchange of information between nations by means of a regular journal.

SCHOOL OF PHARMACY

THE transfer from the Pharmaceutical Society of responsibility for the government of what has lately been known as the College of the Pharmaceutical Society, was announced by Prof. H. Berry, the dean, at the opening of the new session on Oct. 6. The college, which is now reconstituted on an independent basis within the University of London, is to be known as the School of Pharmacy. In addition to the dean, the governing body has the following members:

Nominated by the university.—Mr. O. L. Brady, D.SC., Sir Archibald Gray, F.R.C.P., Mr. J. B. Hunter, F.R.C.S., and Mr. G. B. Jeffery, D.SC., F.R.S.

Nominated by the academic board of the college.—Prof. G. A. H. Buttle, M.R.C.S., Miss Katharine Coward, D.SC., Mr. J. W. Fairbairn, PH.D., and Prof. W. H. Linnell.

Nominated by the Pharmaceutical Society.—Mr. W. S. Howells, Mrs. J. K. Irvine, Mr. H. N. Linstead, and Mr. C. W. Maplethorpe.

Coöpted members.—Sir Henry Dale, O.M., F.R.C.P., Mr. W. J. C. Quarrell, and Sir Harry Jephcott (chairman).

Mr. S. R. Curtis has been appointed secretary to the school.

University of London

At a recent examination for the diploma in medical radiology the following were successful:

J. C. Bulstrode, J. G. L. Cole, J. C. A. L. Colenbrander, J. B. Latto, Daniel O'Connell, J. H. O'Connell, Basil Stoll, R. D. St. G. Tucker, A. H. N. Welikala.

Mr. G. Ewart Martin will deliver the Semon lecture at 1, Wimpole Street, W.1, on Thursday, Nov. 4, at 4 P.M. He has chosen as his subject Broncho-œsophagology in Great Britain.

On Tuesday, Nov. 16, at 5 P.M., Dr. Charles Swan will speak on Rubella in Pregnancy as an Ætiological Factor in Congenital Malformations and Stillbirth; and on Friday, Nov. 26, at 5.30 P.M., Prof. Dugald Baird on Social Factors in Obstetrics. Both lectures will be given at the Westminster Medical School, Horseferry Road, S.W.1.

Royal College of Physicians of London

On St. Luke's Day, Oct. 18, Dr. F. M. R. Walshe, F.R.S., delivered the Harveian oration which is summarised on p. 660. After the oration the Weber-Parkes medal and prize were presented to Dr. S. Roodhouse Gloyne. This prize is awarded triennially for the best work done on the ætiology, prevention, pathology, or treatment of tuberculosis.

1. Spallici, A. *Notiz. Amministrazione sanit.* 1948, **1**, 205.

Digitized by Google

University of Liverpool

On Oct. 15 the following degrees were conferred:

M.Rad.—J. R. MacLeod, D. E. Paterson.

University of Sheffield

Prof. John Chisholm, who has held the chair of obstetrics and gynæcology since 1935, has become part-time director of the department of obstetrics and gynæcology. He will continue to hold his post on the staff of the Jessop Hospital. Dr. William Hobson has been appointed to the new chair of social and industrial medicine.

Dr. Hobson, who is at present senior lecturer in preventive medicine in the University of Bristol, and honorary assistant medical officer of health to the city of Bristol, took his B.SC. at Leeds with first-class honours in 1933. Three years later he took his M.B. and became lecturer in physiology and hygiene in the University of Leeds, a post which he held till 1938, when he was appointed assistant school medical officer for Leeds. The following year, in which he also took his M.D. with distinction, he became assistant M.O.H. for Hampshire, and in 1940 M.O.H. for Lymington. From 1942 to 1946 Dr. Hobson served in the R.A.M.C. as a specialist in hygiene, and he was mentioned in despatches. His published work includes a paper on urinary output of creatine and creatinine associated with physical exercise and its relationship to carbohydrate metabolism.

Mr. Tom Smith has been appointed temporary lecturer in obstetrics and gynæcology, Dr. Jeanne Montgomery assistant to the medical officer for the student health service, and Dr. J. B. Pyper demonstrator in anatomy. Dr. J. A. Kilpatrick, Dr. D. H. Randall, and Dr. J. Maclean Smith have become tutors in medicine, surgery, and medical pathology respectively, and Dr. J. K. A. Beverley and Dr. Sheila M. Stewart honorary demonstrators in bacteriology.

Royal College of Surgeons of England

At a meeting of the council held on Oct. 14, with Lord Webb-Johnson, the president, in the chair, Prof. Geoffrey Hadfield was admitted as Sir William Collins professor of human and comparative pathology, and the John Tomes prize was presented to Prof. H. H. Stones, Liverpool. The fellowship in dental surgery was awarded to Dr. Harvey H. Reid, Canada, and Prof. B. Gottlieb, Austria.

Prof. J. H. Dible was appointed examiner in pathology for the forthcoming primary fellowship examination in Ceylon. Diplomas of membership were granted to R. B. Heisch, C. I. Hood, and D. H. K. Soltau. The following diplomas were granted jointly with the Royal College of Physicians:

D.I.H.—T. S. Adisubramaniam, M. A. C. Dowling, William Gunn, M. N. Gupta, E. T. Harrison, G. O. Hughes, T. H. McCormack, L. E. J. Poulter, J. B. Sherman, J. A. Smiley, J. M. Stuart, A. R. Thompson.

D.T.M. & H.—C. S. Agrawal, M. H. S. E. Amroussi, Norah H. C. Clarke, B. P. Courtenay-Mayers, K. O. Courtney, R. M. Cross, R. S. Dayal, H. G. Edmunds, Walter Fabisch, J. D. Grene, J. T. Harold, G. F. Houston, M. H. Hughes, S. A. Jones, Ronald Lwin, George McHugh, B. U. Mistry, Mok Hing Yiu, Radhagovind Panigrahi, Mariano Rech, A. S. Saffar, M. A. E. Sayed, S. C. Sekar, A. K. Sen, F. K. Shah, W. D. L. Smith, M. L. Sur, Eustachy Tustanowski, G. H. Wattley, Wu Hsueh-Tsung.

D.O.M.S.—R. C. Agarwal, A. N. Ashworth, N. L. Bailey, S. C. Banerji, G. M. Barling, B. A. Bembridge, T. A. S. Boyd, R. S. E. Brewerton, J. B. Bunting, Thomas Chadderton, R. M. Chambers, Shing-Chue Chan, P. M. Chaudhuri, E. S. Dismorr, N. F. Donaldson, Samuel Etzine, J. H. W. Fagan, P. I. Franks, Samuel Galbraith, P. J. A. Gormley, T. B. Gupta, Ko Gyi, Andrew Harrison, J. R. Hudson, P. J. L. Hunter, R. I. Jaffe, K. R. Kesavachar, T. G. Kletz, Maxwell Lerner, H. F. T. MacFetridge, B. A. Marshall, T. S. Maw, Mohammad Mohsin, Louis Myers, W. J. Naunton, M. J. Nikosiewicz, Eithne J. O'Riordan, C. M. Phillips, S. T. Puttanna, J. E. Pyper, J. L. Reiss, Kazimierz Rubinstein, Hamida Saiduzzafar, A. E. Sawday, Mohamed Shaffi, Ellis Shenken, N. I. Sreenivasan, C. S. Swan, Jack Swartz, A. K. Tulloch, J. M. Whaites, P. C. Yates.

D.C.H.—H. C. Allan, Sivasithamparam Balasingam, Marion B. Bethune, Saktipada Bhattacharjee, Camilla B. P. Bosanquet, T. A. Brand, E. J. S. N. Briggs, F. B. Bromfield, H. J. S. Brown, Isobel M. Brown, M. F. G. Buchanan, L. J. Bussell, Helen A. Cawson, A. B. Christie, Margaret T. Collins, W. D. D. Cooke, E. G. A. Crawshaw, J. U. Crichton, P. O. Crossfield, G. H. R. Curnock, William Davies, A. W. Dickie, M. H. C. Dyson, P. D. Fergusson, R. J. L. Ferris, H. J. W. Fisher, I. H. Fletcher, J. O. Forfar, Frances A. Fouracres, Gin Shan-Yah, Janet F. Graham, J. R. Harries, Dorothy A. Harvey, K. W. Hazratji, Betty E. Howarth, B. M. C. Hudson, Pauline M. Jackson, J. C. Johnson, R. St. J. R. Johnston, Gouri Kirtane, Stephanie A. Laing, B. M. Laurance, J. A. Leitch, Richard Lindop, R. H. G. Lyne-Pirkis, Kathleen J. McCarthy, Muriel M. McLean, H. B. Marsden, Margaret St. C. Masson, Gladys A. Meigh, Rachel Menashe, S. M. Merchant, H. R. A. Michelmore, Dorothy J. Miller, R. G. Mitchell, E. S. Monteiro, J. N. Montgomery, Norrene M. Nicholson, W. B. O'Driscoll, E. J. Parr, Jack Pelunsky, A. P. Radford, Elizabeth Radovitch, J. T. Rendle-Short, G. A. V. Ribeiro, Frank Riley, B. S. Rose, D. C. Ryan, Mubarika Shah, Gwendolen D. Smith, Peter Stevens, Basil Strickland, P. V. Suckling, Jean C. Taylor, K. B. Thornton, Joyce F. Tucker, C. H. C. Upjohn, D. F. Van Zwanenberg, D. G. Vulliamy, G. F. Walker, J. M. Watt, L. E. Wear, S. D. V. Weller, R. W. Wilkinson, Jean C. Willison, B. S. B. Wood, L. A. Zeki.

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on Oct. 1, with Sir William Gilliatt, the president, in the chair, the honorary fellowship was conferred on Dr. Emil Novak of Baltimore. Dr. A. F. Hollinrake (Ontario) was admitted to the fellowship, and the following to the membership:

I. S. R. Bain, Henrietta E. Banting, T. L. S. Baynes, Samuel Behrman, D. C. A. Bevis, C. C. Bowley, T. St. V. W. Buss, L. W. Cox, Mary E. Egerton, T. E. Elliot, G. McI. Forsyth, H. D. Freeth, G. T. Gibson, J. H. Gibson, Andrew Graham, A. H. Grenz, Constance A. Grey, H. B. Hattam, C. C. Henneberg, Ebbie Hesselberg, D. W. Higson, J. C. Holman, K. R. Hudson, A. G. Jones, J. B. Joyce, W. T. Kenny, G. G. Kerster, R. A. H. Kinch, Samuel Lask, T. L. T. Lewis, E. L. F. McConnachie, William Macfarlane, J. M. McKiddie, S. H. Madden, Helen M. Mayer, G. W. H. Millington, F. L. E. Musgrove, J. R. Norris, J. J. F. O'Sullivan, J. H. Patterson, A. C. Pearson, W. H. Peek, S. D. Perchard, David Prysor-Jones, E. H. Rees, S. McR. Reid, H. A. Ripman, D. N. S. Robertson, B. W. Sanderson, G. A. Silley, A. A. Smith, Tom Smith, G. J. Sophian, Christine M. Stacey, P. C. Steptoe, C. S. N. Swan, R. A. Thatcher, G. S. Thomas, R. G. Whitelaw, R. M. Williams, M. S. Williamson, H. G. Wolskel, P. S. Wright, R. B. Wright.

A postgraduate course in the practice of obstetrics and gynæcology will be held at the college from Nov. 15 to 19. Further particulars will be found in our advertisement columns.

Royal Medico-Psychological Association

On Friday, Nov. 12, at 2.15 P.M., at 26, Portland Place, London, W.1, Mr. Claud Mullins, late Metropolitan police-court magistrate, will deliver the Maudsley lecture. He is to speak on Psychiatry in the Criminal Courts.

Pharmaceutical Society of Great Britain

Dr. C. H. Hampshire, secretary of the British Pharmacopœia Commission, will speak on the British Pharmacopœia, 1948, at a meeting to be held at 17, Bloomsbury Square, London, W.C.1, on Thursday, Oct. 28, at 7.30 P.M. The lecture will deal generally with the pharmacopœia, as an introduction to a course of seven weekly lectures.

Public Health and Municipal Engineering Congress and Exhibition

Mr. Aneurin Bevan, the Minister of Health, will open this congress and exhibition at noon on Monday, Nov. 15, at Olympia. The Ministries of Works, Food, and Agriculture and Fisheries and the Department of Scientific and Industrial Research, are to be among the 168 exhibitors. The congress and exhibition will continue until Nov. 20.

More Nurses and Midwives

Full-time nursing and midwifery staffs in hospitals in England and Wales have risen by 2000 in twelve months. In June, 1948, the total, including those trained and in training, was 117,000, compared with 115,000 a year earlier. Part-time nursing and midwifery hospital staffs over the same period rose by nearly 7000—from 10,700 to 17,380. These increases have made it possible to reopen beds closed through lack of staff, and of the 63,000 previously out of action for this reason nearly 6000 were again available for patients by June this year. The Ministry of Health says: "The point has now been reached when every addition to the hospital nursing and midwifery staffs means either the opening of more beds or the improvement of working hours and conditions, or sometimes both."

R.S.M. Microfilm Unit

Thanks to a generous grant from the Rockefeller Foundation and the practical help of the Ministry of Health, Board of Trade, and Foreign Office, a finely equipped microfilm unit has been completed at Dering Yard, off Bond Street, for the Royal Society of Medicine. At the inauguration on Monday evening Sir Henry Dale, F.R.S., the society's president, explained that its work of duplicating medical papers and other documents began in the late war, as a scheme for keeping base hospitals informed. Microfilm projectors were provided by the society at hospitals ranging from the Rhine to Delhi, and the Royal Air Force transported the films from London. A Rockefeller endowment in 1945 made it possible to apply the microfilm service to the big task of filling gaps in the journal files of medical libraries in Europe and elsewhere. Already 3500 unobtainable back-volumes of journals have been duplicated and supplied; and it is hoped that the present unit, with its production capacity of 25,000 pages on microfilm a day, will be able to meet the large number of orders still outstanding.

Digitized by Google

No. 2 (Br.) General Hospital

The second reunion dinner for ex-members of this Army unit is being held on Saturday, Nov. 13. The organiser is Dr. J. H. Easton, 42, Pembury Road, Tonbridge, Kent.

Royal Institute of Public Health and Hygiene

Sir Lionel Whitby will deliver the Harben lectures at the institute, 28, Portland Place, London, W.1, on Tuesday, Wednesday, and Thursday, Dec. 7, 8, and 9, at 3 P.M. He is to speak on Hæmopoiesis.

Extra Food for the Tuberculous

The Ministry of Food has explained that patients with active tuberculosis are allowed each week, besides their ordinary rations, 1 oz. of bacon, 1 oz. of cooking fat, and 3 oz. of butter or margarine. They are entitled to three eggs and 14 pints of milk.

W.H.O. Regional Office

A regional office for south-east Asia is shortly to be set up by the World Health Organisation; this will serve India, Ceylon, Thailand, Burma, and Afghanistan. It is proposed that other regional offices should be established for Africa, the Eastern Mediterannean, the Western Pacific, and the American continent.

Rehabilitation: a Course for Foreign Visitors

The British Council is holding a course on Rehabilitation and Resettlement of the Disabled, which began in London on Oct. 18 and which will be continued at Mansfield and Birmingham. Some 20 visitors from Europe and China are attending the course, which was organised in response to requests from specialists in Europe who wished to see what Britain is doing in this field. The medical part of the course has been arranged by Dr. Harold Balme, medical officer in charge of rehabilitation, Ministry of Health.

Polarography in Biochemistry

A discussion on this subject will be held by the polarographic discussion panel of the Society of Public Analysts and Other Analytical Chemists at 3.45 P.M. on Friday, Oct. 29, at the Imperial College of Science and Technology, South Kensington, London, S.W.7. Mrs. A. M. Robinson, PH.D., and Mr. F. L. Warren, D.SC., will speak on Applications of Polarography in the Diagnosis and Treatment of Cancer, Mr. Tudor S. G. Jones, PH.D., on the Determination of Amino-acids by Polarographic Reduction of their Copper Complexes, and Mr. J. E. Page, PH.D., on the Polarography of Penicillin.

Liverpool Regional Hospital Board

At a meeting held on Oct. 7 the board approved an estimate of expenditure for 1949–50 of £7,160,280, of which £597,282 is to be spent on capital work at hospitals. No guidance has been received from the Ministry of Health as to the total expenditure on capital work to be allowed by the board, and it was agreed to acquaint the Ministry with the full needs of the region. The board estimated that works begun in 1949–50 would require a further expenditure of approximately £900,000 in the financial year 1950–51.

The board approved in principle the proposal to erect a first stage of a new mental-deficiency institution at Greaves Hall, Banks, near Southport, at a cost of £2,000,000.

Return to Practice

The Central Medical War Committee announces that Mr. Gilbert Parker, F.R.C.S.E., has resumed civilian practice at 25, The Crescent, Linthorpe, Middlesbrough.

Dr. A. C. Norman has been appointed to the third class (civil division) of the Order of Al Rafidain in recognition of his services as director of the X-ray institute at the Royal College of Medicine, Baghdad.

Major-General R. J. Blackham, M.D., on completion of 21 years' service as clerk of the Worshipful Company of Glaziers and Painters of Glass, has been unanimously elected an honorary member of the court of assistants of the company. The court and livery of the Glaziers Company also presented him with an antique clock and a cheque.

Appointments

CASE, R. A. M., M.B., PH.D. Birm.: fellow, Chester Beatty Institute for Cancer Research, London.

MACKENZIE, N. F., M.B. Edin., DIP. PSYCH.: superintendent, Newchurch Home, Culcheth; adviser to the Liverpool Regional Hospital Board on mental deficiency problems and supervisor of the board's smaller mental deficiency establishments.

RAVEN, R. W., O.B.E., F.R.C.S.: visiting surgeon, Star and Garter Home for Disabled Sailors, Soldiers, and Airmen.

Hospital for Sick Children, Great Ormond St., London:

BLACK, J. A., M.B. Camb., M.R.C.P.: asst. medical registrar, gastro-enteritis flying squad and hospital gastro-enteritis unit.

COWAN, R. J., M.D.: house-surgeon, orthopædic department.

DAVIES, PAMELA, M.B. Glasg.: asst. resident M.O., Tadworth Court.

MACOUN, S. J. R., B.A., M.B. Camb., M.R.C.P.: house-physician.

SAVAGE, T. R., M.A., B.M. Oxfd, M.R.C.P.: house-physician.

London County Council Public Health Department:

Asst. divisional M.O.:

ATLEE, C. N., M.D. Durh., M.R.C.P., D.P.H.

BUTLER, LILY, M.R.C.S., D.P.H.

LOW, J. B., M.B. Edin., D.P.H.

POLHILL, M. C., M.R.C.S., D.P.H.

SIMPSON, R. H., M.D. Lond., F.R.C.P., D.T.M. & H., D.P.H.

Diary of the Week

OCT. 24 TO 30

Monday, 25th

SOCIETY OF APOTHECARIES, Black Friars Lane, E.C.4
4 P.M. Dr. Basil Parsons-Smith: Hypertension.

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W.1
8.30 P.M. Dr. Jack Rubie, Dr. Geoffrey Marshall: Streptomycin.

Tuesday, 26th

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. A. D. Porter: Liver Function in Certain Diseases of the Skin.

INSTITUTE OF LARYNGOLOGY & OTOLOGY, 330, Gray's Inn Road, W.C.1
2.30 P.M. Mr. W. A. Mill: Malignant Diseases and Radiotherapy.

EUGENICS SOCIETY
5.30 P.M. (Burlington House, Piccadilly, W.1.) Mr. Cecil Binney: Legal and Social Implications of Artificial Insemination.

Wednesday, 27th

SOCIETY OF APOTHECARIES
5 P.M. Prof. Henry Cohen: Therapy as a Diagnostic Measure.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY
4.30 P.M. (1, Wimpole Street, W.1.) Dr. J. M. H. MacLeod: Milestones on a Dermatological Journey. (Prosser White oration.)

MEDICO-LEGAL SOCIETY
8.15 P.M. (26, Portland Place, W.1.) Judge Earengey: Criminal Justice.

ROYAL INSTITUTE OF PUBLIC HEALTH & HYGIENE, 28, Portland Place, W.1
3.30 P.M. Dr. C. Fraser Brockington: Problem Families.

UNIVERSITY OF GLASGOW
8 P.M. (Department of Ophthalmology.) Prof. A. Loewenstein: Histopathology of the Drainage Angle.

Thursday, 28th

SOCIETY OF APOTHECARIES
5 P.M. Sir Stanford Cade: Management of Inoperable Malignant Disease.

INSTITUTE OF NEUROLOGY, National Hospital, Queen Square, W.C.1
5 P.M. Prof. E. G. T. Liddell: Integration—Then and Now.

LLOYD ROBERTS LECTURE
4.30 P.M. (St. Mary's Hospitals, Manchester.) Mr. R. M. Titmuss: Parenthood and Social Change.

CHADWICK LECTURE
4 P.M. (University College, Nottingham.) Sir Arthur MacNalty: Advances in Preventive Medicine during the War of 1939–45.

HONEYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Dr. R. G. Gordon: Psychogenic Pain.

Friday, 29th

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES
8 P.M. (11, Chandos Street, W.1.) Mr. Reynold Boyd: the V.D. Factor in Infertility and Sterility and its Treatment.

Saturday, 30th

BIOCHEMICAL SOCIETY
11 A.M. (London School of Hygiene, Keppel Street, W.C.1.) Symposium on Partition Chromatography and its Application to Biochemical Problems. (This notice was incorrectly included in last week's Diary.)

CORRIGENDUM: *Conference on Infertility.*—The substance used by Dr. Ernst Friedman in hysterosalpingography (*Lancet*, Oct. 2, p. 543) is 'Viskiosol 6,' made by Messrs. May & Baker, Ltd.

Digitized by Google

OCT. 30, 1948 PAGES 675 TO 714

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6531 LONDON: SATURDAY, OCTOBER 30, 1948 CCLV

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Treatment of Thyrotoxicosis
Sir CARRICK ROBERTSON, F.R.C.S. 675

Meningococcosis: a Protean Disease
H. STANLEY BANKS, F.R.C.P. (*concluded*) 677

Infection Through Soaked Dressings
LEONARD COLEBROOK, F.R.C.O.G., F.R.S.
A. M. HOOD 682

A Method of Testing Analgesics in Man
A. J. H. HEWER, M.B.
C. A. KEELE, F.R.C.P. 683

Nebulised Penicillin and Post-operative Pulmonary Complications
E. J. HOLBOROW, M.B.
E. A. SPRIGGS, M.R.C.P. 688

Tuberculous Mastoiditis Treated with Streptomycin
O. D. FISHER, M.B.
E. A. MALKIN, M.R.C.S. 689

PRELIMINARY COMMUNICATION

Trigeminal Neuralgia Treated with Cuprelone
A. M. G. CAMPBELL, M.R.C.P. 690

SPECIAL ARTICLES

Rehabilitation in Industry
L. W. PLEWES, F.R.C.S.E.
J. N. BARRON, F.R.C.S.E.
A. R. THOMPSON, M.D.
H. H. NEWELL 699

Academic Salaries 703

PUBLIC HEALTH

Home Nursing of Premature Babies in Newcastle-on-Tyne
F. J. W. MILLER, M.R.C.P. 703

Births and Deaths in the Third Quarter 705

Births in the U.S.A. 705

Encephalitis in Japan 705

LEADING ARTICLES

BLOOD FOR TRANSFUSION 693

SPECIFICITY OF INFECTION 694

RETURN TO PHILANTHROPY? ... 695

ANNOTATIONS

Infant Morbidity 696

Gastro-enteritis Flying Squad ... 696

In the Mines 696

Streptomycin Resistance and Dependence 697

Asiaticoside in Leprosy 697

The Ballistocardiogram 697

Ordinary Girls 698

Sympathectomy and the Heart .. 698

LETTERS TO THE EDITOR

Infantile Gastro-enteritis and Streptomycin (Dr. C. Giles) ... 706

Recurrent Dislocation of the Shoulder (Mr. A. S. B. Bankart, F.R.C.S.) 706

Beds for Pulmonary Tuberculosis (Dr. W. H. Tattersall) 707

Unfortunate Names of Hospitals (Dr. Ronald MacKeith) 707

Hyaluronidase and Gonorrhœal Infection (Dr. F. L. Lydon) ... 707

Dentures and Anæsthesia (Mr. E. H. Phillips; Dr. D. D. C. Howat) 708

Carotid-sinus Syndrome (Prof. F. J. Nattrass, F.R.C.P.) 708

Deeper and Deeper (Surgeon Captain Gustaf Severin, R.S.N.) 708

Dosage of Sulphetrone for Children (Dr. J. L. Emery) 709

Production of Insulin (Mr. J. C. Hanbury) 709

Psychogenic Rheumatism (Dr. I. H. Milner) 709

Proprietary Medicines under the National Health Service Act (Dr. A. Forster) 709

Compulsory Admission (Dr. T. St. M. Norris) 709

Convalescence: Fee or Free? (Dr. E. Hinden) 710

Letter to a Nephew 710

NEW INVENTIONS

Dissecting Forceps with Spatulate Ends
RODNEY MAINGOT, F.R.C.S. .. 691

REVIEWS OF BOOKS

Cardiography. William Evans, F.R.C.P. 692

Recent Advances in Surgery. H. C. Edwards, F.R.C.S. 692

Practical Bacteriology, Hematology, and Parasitology. E. R. Stitt, M.D., and others 692

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 705

OBITUARY

Percival Pasley Cole 710

Henry Smith 711

The late Dr. Western 711

NOTES AND NEWS

Training Grants for Assistants .. 712

Glasgow and its Royal Faculty. 712

Icy Christmas 712

Prevention of Deafness 712

Rh 712

Food Rations in Germany and Austria 712

The Haven Products Scheme 712

University of Oxford 713

University of Cambridge 713

University of London 713

University of Liverpool 713

University of Leeds 713

Royal College of Physicians of London 713

Royal College of Surgeons of England 713

University College, London 713

Institute of Laryngology and Otology 713

Blackcurrant Syrup 714

Contamination of Food by Metals 714

Priority for Children's Teeth 714

Diary of the Week 714

Appointments 711

Births, Marriages, and Deaths .. 714

A SELECTION OF LIVINGSTONE'S LATEST PUBLICATIONS

C. ALLAN BIRCH. **EMERGENCIES IN MEDICAL PRACTICE.** 25s.

W. S. C. COPEMAN. **TEXTBOOK OF THE RHEUMATIC DISEASES.** 50s.

F. CROXON DELLER. **THE MODERN MANAGEMENT OF GASTRIC AND DUODENAL ULCER.** 20s.

ERNEST MUIR. **MANUAL OF LEPROSY.** 17s. 6d.

ARTHUR NAYLOR. **FRACTURES AND ORTHOPÆDIC SURGERY FOR NURSES AND MASSEUSES.** 17s. 6d.

H. J. PARISH. **BACTERIAL AND VIRUS DISEASES: Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment.** 7s. 6d.

HUBERT H. STONES. **ORAL AND DENTAL DISEASES: Ætiology, Histopathology, Clinical Features and Treatment.** 90s.

F. M. R. WALSHE. **CRITICAL STUDIES IN NEUROLOGY.** 15s.

H. P. WINSBURY-WHITE. **TEXTBOOK OF GENITO-URINARY SURGERY.** 90s.

* TWO FORTHCOMING BOOKS WORTHY OF NOTE *

ATLAS OF NEUROPATHOLOGY. By WM. BLACKWOOD, F.R.C.S.E., T. C. DODDS, F.I.M.L.T., and J. C. SOMMERVILLE, A.I.M.L.T. 35s.

INTRODUCTORY BOTANY. By ALEXANDER NELSON, B.Sc., Ph.D. 21s.

16-17, TEVIOT PLACE, EDINBURGH — 45, LINCOLN'S INN FIELDS, LONDON

Digitized by Google

OXFORD MEDICAL

PUBLICATIONS

JUST PUBLISHED

A NEW (FIFTH) EDITION OF

POST-MORTEM APPEARANCES

By JOAN M. ROSS, M.D., B.S., M.R.C.S., L.R.C.P.

Adviser in Pathology to the Ministry of Supply; late Reader in Pathology, University of London; Morbid Anatomist to the Royal Free Hospital; Assistant Pathologist to St. Mary's Hospital

Contents include: General Remarks—Death from Causes other than Disease—General Metabolic and Deficiency Diseases—General Infections—Diseases of the Digestive System—Diseases of the Kidney—Diseases of the Respiratory System—Diseases of the Ductless Glands—Diseases of the Blood and Blood-forming Organs—Diseases of the Cardio-vascular System—Diseases of the Nervous System—Still Births and Neonatal Deaths—Anatomical Normals (Averages)—Length and Weight of Fœtus—Approximate Weight of Organs of Newborn Child—Dates of Ossification of Principal Bones—Ages of Eruption of Teeth—Age of Fœtus—Changes in Umbilical Cord—Index.

318 *pages* 8*s.* 6*d. net*

THE BACKGROUND OF THERAPEUTICS

by J. H. BURN, *M.D., F.R.S.* 376 *pages* 59 *illustrations* 26 *tables* 22*s.* 6*d. net*

THE NATURAL HISTORY OF DISEASE

by JOHN A. RYLE, *M.A., M.D., F.R.C.P. Second Edition* 498 *pages* 9 *illustrations* 22*s.* 6*d. net*

CHANGING DISCIPLINES

by the same Author. 140 *pages* 13 *illustrations* 10 *tables* 12*s.* 6*d. net*

MANAGEMENT IN OBSTETRICS

by ANDREW M. CLAYE, *M.D., F.R.C.S., F.R.C.O.G.* 196 *pages* 17 *illustrations* 12*s.* 6*d. net*

ELEMENTS OF SURGERY

by FAUSET WELSH, *B.Sc., M.B., F.R.C.S. With a Foreword by* SIR CECIL WAKELEY, *K.B.E., C.B.* 88 *pages* 7*s.* 6*d. net*

PSYCHOTHERAPY: ITS USES AND LIMITATIONS

by D. R. ALLISON, *M.D., M.R.C.P., and* R. G. GORDON, *M.D., D.Sc., F.R.C.P.* 168 *pages* 8*s.* 6*d. net*

MAJOR ENDOCRINE DISORDERS

by S. LEONARD SIMPSON, *M.A., M.D., F.R.C.P. Second Edition* 574 *pages* 122 *illustrations* 42*s. net*

OBSTETRICS AND GYNÆCOLOGY

by C. SCOTT RUSSELL, *M.B., F.R.C.S., M.R.C.O.G. With a Foreword by* J. CHASSAR MOIR, *D.M., F.R.C.S., F.R.C.O.G.* 222 *pages* 21 *illustrations* 12*s.* 6*d. net*

OXFORD UNIVERSITY PRESS

Digitized by Google

TREATMENT OF THYROTOXICOSIS

REVIEW OF 350 CASES

SIR CARRICK ROBERTSON
M.B. Lond., F.R.C.S., F.R.A.C.S.
CHIEF OF STAFF, MATER MISERICORDIÆ HOSPITAL, AUCKLAND, NEW ZEALAND; CONSULTING SURGEON, AUCKLAND HOSPITAL

THIS paper is based on clinical observations on 350 cases of thyrotoxicosis treated between January, 1945, and September, 1947.

During this period all patients with thyrotoxicosis have had suggested to them trial of the thio compounds, whenever it was thought likely that they would benefit—but here lies the difficulty. At first there were no criteria to guide one, and even now there are too few; but, as experience grows, it is becoming a little easier to advise patients which course to pursue.

Of the 350 only 111 were treated with thiouracil; so in this series the scales are rather heavily weighted on the surgical side, the reasons being that many of the patients were sent by practitioners as cases for operation, or the patients had already decided that they preferred surgery to protracted medical treatment.

These 111 patients treated with thiouracil have been divided into three age-groups, since the younger patients seem more often to achieve a permanent cure on thiouracil than do the older ones:

Age-group (years)	*No. of patients*	*No. improved*
Under 21	16	10 (62%)
21–45	73	29 (40%)
Over 45	22	11 (50%)
	111	50 (45%)

In the last group all the goitres were nodular and most of the patients had been thyrotoxic for years; many were bad surgical risks. The 11 patients who improved were very pleased with the result, in spite of the fact that they still had palpable and visible goitres and some were not entirely cured of fibrillation. Apart from these 11 were others who had, in addition, a very high blood-pressure. All of these hypertensive thyrotoxics were treated with thiouracil, and in none was the blood-pressure lessened, nor did the treatment raise any enthusiasm on the part of the patient. Those who subsequently underwent operation professed themselves much better, though there was still no great difference in the hypertension—perhaps a somewhat similar experience to that found in cases of hypertension treated by sympathectomy. The only thing this age-grouping shows is a slightly better response to thiouracil in the youngest group.

CONTRA-INDICATIONS TO TREATMENT WITH THIOURACIL

On reviewing the failures of this treatment we are now reasonably certain that the following are contra-indications to the use of thiouracil:

(1) *Signs of Pressure on the Airway.*—In nearly every case the goitre enlarges in the first few weeks of treatment with thiouracil. I have seen it stated that enlargement only takes place when too large a dose of thiouracil has been given, but I cannot altogether agree with this statement. I believe that, whatever dose is given, enlargement usually follows. A microscopical section of a thyroid gland in a patient taking thio compounds shows hyperplasia of the cells lining the vesicles as great as, and similar to, that seen in Graves's disease or primary thyrotoxicosis. Therefore the first contra-indication to the exhibition of thiouracil is any pressure on the airway. This obstruction may be obvious to the merest tyro, as in the cases with lateral displacement of the trachea or those with whistling inspiration, but even in a small goitre an insignificant nodule (see below) or a high upper pole (see below), unseen and impalpable because of its retrotracheal position, can cause considerable discomfort, which will be made worse when the goitre is increased by the administration of thiouracil. This is a cogent reason for preferring surgery, with its almost negligible risk, for all nodular goitres.

(2) *Toxic Nodular Goitre.*—All elderly patients with a toxic nodular thyroid gland have grown up with their goitre and little realise how ill they have become, because the change from simple to toxic goitre is slow and insidious. They are bad surgical risks and doubtless should be given the opportunity of thio treatment, but it must be granted that operation more quickly relieves shortness of breath by rapid improvement in the heart action and by removal of pressure on the airway. However ill these patients look when first seen, it is surprising how often they become safe risks after a week or ten days in hospital under suitable medical treatment; if they do not improve in that time, they are not safe risks. It is in these cases, and these cases only, that we practise a two-stage operation; and, if one's mind is made up before the surgical attack that a two-stage operation is safer, it is well to stick to that opinion, however easy and simple the first half of the operation may be. My own opinion is that toxic nodular goitre should be treated by surgery with very few exceptions.

There is little difference between the toxic symptoms of the hyperplastic and of the toxic nodular thyroid glands. Microscopically the nodular goitre is seen to have hyperplastic tissue in the parts of the nodules or surrounding tissue similar in all respects to the hyperplasia seen in Graves's disease. So, if thiouracil is good for one, why not for the other? The answer is that, though the symptoms may be relieved, the patient is not satisfied; and I offer the following explanation.

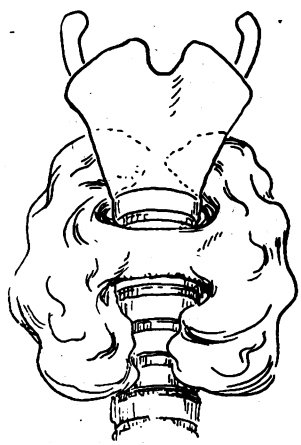


Diagram of upper poles of a toxic goitre winding round the back of the larynx. The right upper pole contains a small nodule or adenoma.

It is not uncommon to see, at operation on a large nodular goitre, an indentation or softening of the trachea as the result of pressure. But it does not appear to be commonly recognised that, even in small nodular goitres, a small nodule in the deeper part of the thyroid gland may have insinuated itself between the vertebræ and the œsophagotracheal tract. This cannot be seen or palpated until the gland has been exposed at operation. Whenever a nodule is found behind the trachea, it is shiny, glistening, and greyish, like a waterworn stone. Probably this appearance is due to thickening of the capsule by the up and down movement of the trachea during swallowing. In these cases there is no indentation of the trachea, but the nodule or the enlarged upper pole must cause discomfort, such as a tight feeling in the neck, often more obvious during swallowing.

(3) *Retrolaryngeal Upper Pole of Thyroid Gland* (see figure).—Several patients with hyperthyroidism and little apparent goitre, but only the smooth gland of Graves's disease, were treated with thiouracil for 2–4 months but refused to carry on and demanded surgery. They found difficulty in explaining why. According to the basal metabolic rate (B.M.R.) they should have felt better, but they were obviously unhappy and had an ill-defined discomfort in the neck—a sort of goitre-consciousness. At first it was thought that they were

Digitized by Google

not making sufficient effort or were becoming neurotic. When the thyroid gland was exposed at operation, it was found that, though the gland was small, high upper poles were lying behind the larynx and pharynx. Their appearance was similar to that of a retrotracheal nodule as already described.

(4) *Pronounced Exophthalmos* (approaching the malignant type).—This is usually found in people over 35 years of age and is accompanied by œdema of the eyelids. We have given a few of these cases serious trials of thiouracil, but none improved and, as the B.M.R. became less, the exophthalmos increased. In the type of exophthalmos seen in patients under the age of 30 years with Graves's disease the protrusion of the eye subsides equally with the subsidence of the toxic symptoms, whether treated by thiouracil or by surgery.

(5) *Predominance of Heart Symptoms* (e.g., tachycardia and fibrillation).—These are the last symptoms to improve on thio compounds—it may take months, as opposed to the quick results of surgery.

(6) *Depression due to Thyrotoxicosis.*—The thio compounds, like the sulphonamides, are inclined to cause depression in some patients.

(7) *Absence of Facilities for Blood-counts, &c.*—If patients have to come in to a centre where there are such facilities, then the economic question is to be considered, since they have to give up work for a much longer time than has the average surgical case.

We have seen one patient die as a result of thiouracil. She was a woman of 50 sent into the hospital from a country district as an acute cholecystitis. A blood-count showed a complete absence of white cells. It was then discovered that she had been treated for two months with thiouracil for thyrotoxicosis. In spite of all treatment, including parenteral penicillin, she died in three or four days.

INDICATIONS FOR TREATMENT WITH THIOURACIL

The following are indications for the use of thiouracil:

(1) *Young People with Graves's Disease.*—At this age nodulation is only just beginning; therefore difficulties arising from increase in size of the thyroid gland are not common, except in those with high retrolaryngeal upper poles.

(2) *Predominance of Nervous Symptoms except Depression.*—There is no doubt that a quicker improvement of the nervous flushes and excitement takes place with thiouracil compounds than with iodine.

(3) *Elderly people who are grave surgical risks.*

(4) *Recurrent Thyrotoxicosis after Operation.*—These cases often respond quickly to 0·2–0·3 g. of thiouracil daily, but we have had several failures because the swelling of the thyroid remnant has been increased by the administration of thiouracil and caused a choking feeling. (In our method of thyroidectomy a small piece of the posterior part of the thyroid gland is left lying closely along each side of the posterolateral aspect of the trachea.)

Preparation for Operation.—Severe thyrotoxicosis may be benefited by preoperative treatment with thiouracil. As a rough guide it is said that one day of treatment will be needed for each percentage of elevation in the B.M.R. This means that a patient with a B.M.R. of 90% would take 90 days of preparatory treatment and, at the end of that time, would have to have two weeks' treatment with iodine to make the operation less difficult. There is no doubt that a thiouracil-prepared case is more difficult than one which has not been so prepared. The use of iodine makes the gland less vascular and firmer and so easier to operate on. Altogether this subjects the patient to a long period of preparation.

Personally, I can see no advantage over the old iodine preparation, combined with rest and sedatives, which will enable a patient with a B.M.R. of 100% to be ready for operation in 10 days or so.

Two years ago, reporting on the result of treatment of 45 cases with thiouracil, I was able to say that 50% had done well.[1] Since that date 6 of these have relapsed and 3 have been operated on; hence the percentage of recovery of these original cases is now only 35%.

1. Robertson, C. *N.Z. med. J.* 1946, **45**, 216.

It seems that thiouracil treatment should be continued for a year or even two. All this time the thyroid gland is kept in a state of cellular activity, as shown in histological sections. In spite of this activity the thyroid gland cannot manufacture its normal hormone; and this may have harmful results, for Purvis and Guisbach [2] have produced adenocarcinoma of the thyroid gland in rats by continued administration of thiourea for two years.

TREATMENT BY SURGERY

Nearly all the failures in all groups were submitted to surgery, making with those operated on without trial of thiouracil over 250 cases. Of the patients under 21 years of age 16 were operated on and only 14 did well. The other 2 were not good results and were given a postoperative course of thiouracil. On this they improved a good deal but are not entirely satisfactory yet. In the age-group 21–45 all the patients operated on did well. Of those aged over 45 all did well except a woman, aged 70, who had been treated with thiouracil for over a year.

She had made great improvement, regarded herself as cured, and stopped taking the drug. I was asked to see her again nine months later. The nodules in the neck had become hard and firm, and she again had thyrotoxicosis. Chiefly because of the hardness of the gland, which suggested a malignant change, operation was advised. She died from abdominal distension the day after operation. The sections from this gland were not malignant but showed severe thyroiditis.

This was the only death in the series, making the surgical mortality well under $^1/_2$%.

SUMMARY

Of 350 patients with thyrotoxicosis 111 were treated with thiouracil: of those aged under 21 years 10 out of 16 (62%) were improved; of those aged 21–45 years 29 out of 73 (40%) were improved; and of those aged over 45 years (all with nodular goitre) 11 out of 22 (50%) were improved.

Contra-indications to the use of thiouracil are signs of pressure on the airway, toxic nodular goitre, a retrolaryngeal upper pole of the thyroid gland, pronounced exophthalmos, predominance of heart symptoms, depression due to thyrotoxicosis, and the absence of facilities for blood-counts, &c.

Indications for the use of thiouracil are the youth of the patient, predominance of nervous symptoms other than depression, elderly patients who are grave surgical risks, recurrent thyrotoxicosis after operation, and severe thyrotoxicosis requiring preparation for operation.

Over 250 patients with thyrotoxicosis, including nearly all those who did not respond sufficiently to thiouracil, were operated on: of those aged under 21 years 14 out of 16 did well; of those aged 21–45 years all did well; and of those aged over 45 years all did well except one who died (the only death in the series).

2. Purvis, H. D., Guisbach, W. E. *Brit. J. exp. Path.* 1947, **28**, 46.

"... The whole world is in a state of unrest: countries, peoples, nations, institutions, are being swept by violent winds; heavy gales are blowing everywhere.... Previously the roots of our being remained steady in the depths even though the boughs swayed and tossed above. Now we begin to feel that fear-making loosening of roots. It is not too much to say that every institution, every individual is now faced with the challenge 'Look to your roots.' It is there that we will find a new wisdom in the original necessity out of which our institutions and tradition grow. Problems of Good and Evil, God and Devil could in the days of our fathers be dealt with in traditional ways, often by traditional admonitions. Now this does not suffice, and we find it imperative to look into things previously avoided as unwholesome, or even unclean. 'Get thee behind me, Satan'—meaning 'Get you back into the unconscious'—is no longer effective."—Dr. C. M. BARKER, in lecture no. 50 of the Guild of Pastoral Psychology.

Digitized by Google

MENINGOCOCCOSIS

A PROTEAN DISEASE*

H. STANLEY BANKS
M.D. Glasg., F.R.C.P., D.P.H.
PHYSICIAN-SUPERINTENDENT, PARK HOSPITAL, HITHER GREEN

(*Concluded from p. 640*)

Complications and Sequelæ

Not only the varieties of meningococcosis but also what are usually termed its complications bear witness to the protean nature of this infection. Complications have been considerably reduced both in number and scope by chemotherapy. For example, pericarditis and neuroradiculitis, formerly not uncommon, were not observed in my series of 706 cases. The most significant reduction, however, is in hydrocephalus and the chronic form of the disease. The three most common complications now are labyrinthitis, arthritis, and cranial-nerve palsies, and, of these, only labyrinthitis leaves sequelæ. The permanent deafness resulting from labyrinthitis is by far the most important residuum among those who recover from the disease.

LABYRINTHITIS

Labyrinthitis is due to infection of the perilymph through its direct connexion with the subarachnoid space. As a rule both vestibule and cochlea are affected. The vestibular lesion produces a defect of balance which remains until it is compensated by re-education of proprioceptive and visual mechanisms, usually after a few months. The cochlear lesion affects the organ of Corti totally or partially, producing perception-deafness (nerve-deafness). Unfortunately the damage is done at an early stage of the disease, commonly on the second or third day; so the chances are against recovery from deafness, even with prompt sulphonamide therapy. In my experience the deafness is transient for a few days or weeks in about 1 in 6 of all cases in which deafness is noted in the acute stage. In a minority of the remainder improvement takes place for a few weeks, or rarely for a few months, after the onset. Permanent deafness in one or both ears, total or partial, is the sad lot of all but the transient cases, and most of them are in children or young adults. In my series the risk of contracting deafness appeared to be about 5–7% in all age-groups except 15–30 years, at which age it was considerably lower:

Age-group	*No. of cases*	*Deafness*	
0–4	242	9 (3·7%)	(5·0%)
5–14	90	7 (7·7%)	
15–29	220	6 (2·7%)	
30–44	88	7 (7·9%)	
45–59	46	3 (6·5%)	
60 and over	20	1 (5·0%)	
Totals	706	33 (4·7%)	

The deafness affects the higher pitched tones, including the whole range of human speech. Low tones and vibrations may be perceived but not clearly distinguished. Tinnitus occasionally accompanies the deafness but is not usually troublesome. The incidence of deafness has often been estimated at about 2% at the time of discharge from hospital (Harries 1942, Joe 1942, Beeson and Westerman 1943). This is an underestimate for the following reasons: (1) deafness in infant patients may not be detected until the second year of life; and (2) unilateral deafness may not be detected until some time after the patient's discharge from hospital, unless each ear of every patient is carefully tested separately before discharge from hospital. In a follow-up of 1075 cases in the London region Maddock (1943) reported 37 cases (3·4%) of partial or total deafness, and in a similar follow-up in South Wales the figure was 5·5% (Degen 1945). In my series 29 cases of deafness were detected in hospital and 4 cases after discharge, a total incidence of partial, total, unilateral, or bilateral permanent deafness of 4·7%. About half of these cases had total bilateral deafness:

Type of deafness	*No. of cases*
Transient	7 (1·0%)
Permanent:	
Unilateral partial	6 (0·8%)
,, complete	5 (0·7%)
Bilateral partial	6 (0·8%)
,, complete	16 (2·3%)
Total permanent	33 (4·7%)

ARTHRITIS, BURSITIS, AND TENOSYNOVITIS

There were 33 cases (4·7%) of joint complications in the series. The joints affected were the shoulder, elbow, wrist, small joints of hand, and knee. Occasionally bursæ in the neighbourhood of joints and tendons at the back of the wrists were affected. The synovial fluid was often turbid, but meningococci could not be grown from it owing to efficient chemotherapy. Resolution was nearly always complete in a few weeks, but occasionally knee, elbow, and shoulder arthritis persisted for some months.

CRANIAL-NERVE PARALYSIS

Lower-motor-neurone Type.—Most commonly this paralysis involved the sixth nerve, then the seventh, third, and fourth in that order. It is probably due to pressure of meningeal exudate on the nerves as they emerge from the brain stem. The duration of paralysis varies from a few days to about four months, the average being two to three weeks, and it always clears completely. In the series there were 16 cases of unilateral and 4 of bilateral external-rectus, 11 of facial, 4 of oculomotor, and 1 of superior-oblique paralysis, a total incidence of 5·2% of lower-motor-neurone cranial-nerve palsies.

Upper-motor-neurone Type.—Cranial nerve paresis of this type is occasionally seen in encephalitic cases. It is usually much more transient than the lower-motor-neurone types. In the present series there were 5 such cases of facial paresis, and there were also one or two cases of transient ptosis of doubtful origin.

NEURITIS OR RADICULITIS

Pressure of exudate on spinal nerve-roots occasionally gives rise to flaccid paralysis of single muscles or muscle groups, but no example of this occurred in the series. It has to be distinguished from sciatic palsy due to the injection, through ignorance or error, of irritating material—e.g., sodium sulphapyridine—into the theca. In the early days of sulphonamide therapy this mistake occasionally caused permanent foot-drop.

HEMIPLEGIA, SPASTIC PARALYSIS, AND JACKSONIAN CONVULSIONS

These are usually due to pressure on the cerebral cortex in the early acute stage when purulent exudate is at its maximum, but they may be due to encephalitic lesions. Since efficient chemotherapy has been used they have become relatively rare and usually transient. In the present series there were 10 cases, including 3 of hemiplegia, among 654 recovered cases. In 1 exceptional case which was fatal, hemiplegia was due to focal hæmorrhage in the internal capsule.

THROMBOSIS OF SUPERIOR LONGITUDINAL SINUS

This is a rare and unexpected catastrophe; 1 case occurred in my experience.

* The Milroy lectures to the Royal College of Physicians for 1945. Deferred because of the author's service overseas.

Digitized by Google

A girl, aged 4 years, was admitted with a moderate attack of the ordinary form; group-II meningococci were cultivated from the spinal fluid; forty-eight hours after admission, when she seemed much improved and the spinal fluid was sterile, she had a sudden attack of vomiting and restlessness; rapid respirations and coma developed, and she died two days later.

At necropsy there was a clearing meningitis, thrombosis of the superior longitudinal sinus, and hæmorrhage into the left frontal lobe. The source of the thrombosis was presumed to be the meningococcal vascular lesion.

OPHTHALMIA

Hyperæmia of the conjunctiva with photophobia often accompanies meningococcal meningitis.

Purulent conjunctivitis may occur as a presenting symptom of meningococcal disease in otherwise healthy subjects or as a complication.

Iridochoroiditis is a more frequent complication. It was noted in 7 cases (1%) in the series. In a woman of middle age the condition progressed rapidly to panophthalmitis, with loss of the eye. In another case pus was observed for two or three days in the anterior chamber, but complete recovery ensued. In 2 young children with iridochoroiditis in the early acute stage of the disease the media were semi-opaque, with 100% loss of light reflex. These 3 cases cleared completely under sulphathiazole treatment.

Blindness may result from (1) iridochoroiditis developing to panophthalmitis, (2) acute optic atrophy apparently associated with pressure of meningeal exudate at the optic chiasma, (3) the optic atrophy of chronic hydrocephalus, or (4) a central lesion in the occipital lobe. All forms are now rare. The incidence of permanent blindness in Beeson and Westerman's (1943) analysis of 3575 case-records was 0·11% and in my series 0·14%.

RETENTION OF URINE

This often presents a considerable problem, especially in men. Restlessness and a tendency to get out of bed may be partly due to a subconscious desire to urinate. Retention of urine soon leads to symptoms of uræmia. The blood-urea should be frequently tested until urine is passed freely. Uræmic coma may tip the scale against the survival of elderly patients. An indwelling catheter is a good precaution against uræmia in difficult cases.

DEHYDRATION

This tends to occur in children and delirious patients owing to the difficulty in giving fluids. Vomiting increases the tendency, and this was a particular danger when sulphapyridine was used in treatment.

CARDIAC COMPLICATIONS

Toxic myocardium is always present in some degree in the acute stage. It was particularly evident as a direct effect of the toxæmia in 4 cases (0·6%) of my series. These were in young people aged 2, 6, 16, and 24 years. They all showed evidence of cardiac dilatation. In 3 cases the auricles were fibrillating for two or three days, and in 1 patient aged 6 years a well-marked *bruit de galop* persisted for three days. All 3 cases rapidly recovered after the infection had been overcome by chemotherapy. In elderly people with myocardial degeneration the toxic effect of the acute disease on the myocardium is less readily assessed.

Pericarditis should be carefully looked for; it may be found unexpectedly at necropsy. *Endocarditis* is rare.

GLYCOSURIA

Pressure of exudate on the floor of the fourth ventricle may occasionally cause glycosuria, which may be associated with severe acetonuria and even coma and has then to be distinguished from concurrent true diabetic coma. In diabetic coma a history of diabetes and the presence of dehydration, low ocular tension, low blood-pressure, high blood-sugar and well-marked ketonuria are significant points. In my series 5 cases of glycosuria and 1 of concurrent diabetic coma were noted.

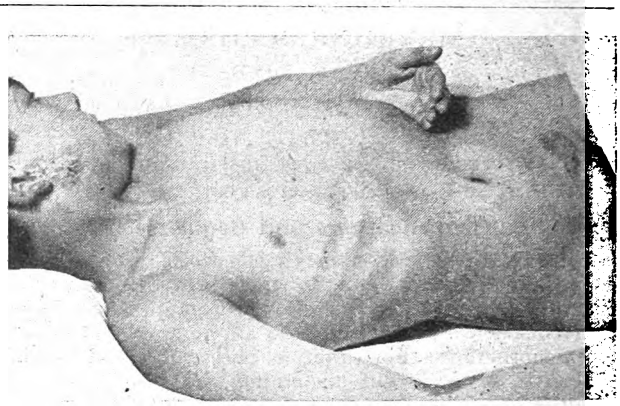


Fig. 11—Extensive herpes febrilis on face, left thumb, and left side of groin, probably spread by contact.

HERPES FEBRILIS

This is a frequent accompaniment, usually from the fourth or fifth day of the disease; it is usually confined to the labial region but is occasionally more extensive. It may involve the face, palate, hand, arm, neck, and even parts of the trunk and lower limbs. This extensive herpes is sometimes regarded as herpes zoster, but it is very exceptional for it to correspond exactly to the distribution of a particular nerve. Rolleston (1919) referred to it as herpes of zoster type. It is unlikely that the chickenpox virus, which is the usual cause of herpes zoster, would often accompany meningococcal disease, whereas the virus of herpes febrilis is well known to be associated with meningococcal, pneumococcal, and acute respiratory infections. Of 10 cases of extensive herpes observed in my series the sites affected were all within easy reach of the patient's hands. In 2 cases the patient's thumbs were affected besides the face and trunk or knee. In no case did the area covered by the lesions correspond exactly to the distribution of a cutaneous nerve or nerves. When herpes in this disease extends beyond the labial region it may have been spread to the new site by the patient's hands (fig. 11). In one of my cases, a virus of herpes febrilis type was isolated from the vesicular fluid by Dr. F. O. McCallum.

ULCERS OF SKIN AND SUBCUTANEOUS TISSUE

These occasionally result from the breaking down of massive purpuric lesions owing to the growth of meningococci within those lesions. If such lesions become secondarily infected, considerable scarring, even of a keloid nature, may result.

RESPIRATORY COMPLICATIONS

Bronchopneumonia is a not uncommon associated condition, especially in infants. The combination is very serious. Some cases are meningococcal in origin, but most are probably due to a secondary pneumococcal or hæmolytic streptococcal infection. Several of my cases of concurrent pneumonia and meningitis were in infants aged 2 or 3 months, who appeared to be saved by the combined use of chemotherapy and the oxygen tent.

Pleurisy is very rare. *Empyema* was found in 1 case.

HYDROCEPHALUS AND ARACHNOIDITIS

These result from subarachnoidal adhesions due to insufficient or delayed therapy in the acute stage. Formerly this was relatively common in infants. Such

Digitized by Google

infants passed through the intermediate stage known as posterior basal meningitis, in which the exudate, after the acute stage, collects at the base of the brain and slowly becomes organised, with the formation of adhesions and subarachnoid block.

In adults, under the same conditions of missed diagnosis and delayed treatment, hydrocephalus may develop, with chronic headache as a symptom. Later, in such cases, there is a tendency for exudate to collect in the dependent dorsal region of the cord, with the formation of adhesions, pressure on nerve-roots, and possibly paraplegia. In such a condition a spinal tap may be dry or yield a small quantity of xanthochromic cerebrospinal fluid (C.S.F.) of very high protein content—e.g., 1 g. per 100 ml. (Froin's syndrome of spinal block). In my series there were 10 (1·4%) cases of hydrocephalus or severe arachnoiditis. Of these, 6 were in infants and 4 in adults. When admitted to hospital these patients were all in the second or third week of the disease, the diagnosis having been missed in the early acute stage. Of the 6 infants 3 died, 1 developed chronic hydrocephalus, and 2 made a perfect recovery. Of the 4 adults 2 died and 2 recovered completely.

Delayed arachnoid clearing without adhesions and without symptoms—e.g., where the C.S.F. shows a pleocytosis of 10–30 cells per c.mm. some weeks after the acute stage—is of little significance. It normally accompanies resolution in some cases and should be disregarded.

RARE COMPLICATIONS

Orchitis and epididymitis are now very rare. I have not seen a case. Other rarities are *salpingitis, jaundice,* and *paralytic ileus*; 1 case of jaundice and 1 of paralytic ileus occurred in my series. *Otitis media* is due to secondary infection and is rare.

RELAPSES AND RECURRENCES

Relapse or recrudescence occurring within a few weeks of the primary attack was formerly common. With efficient sulphonamide treatment it is now uncommon; 3 cases occurred in the series.

Second Attacks.—Immunity does not seem to be solid or permanent in meningococcal disease; 4 second attacks were noted in the series, one, two, three and twenty-five years after the first attack.

SEQUELÆ

By far the most common permanent sequela of organic origin is deafness. Others include hydrocephalus, blindness, and paralyses of various kinds. The group of so-called psychiatric sequelæ were intensively studied in the late war. They are partly of organic origin but can be intensified and fixed by wrong psychiatric handling, especially in war-time when escape from military service becomes a strong subconscious motive. The most common symptom is persistent headache. As a rule this is intermittent, lasting a day or two, and followed by normal intervals of a few weeks; the attacks may recur for as long as eighteen months. The headache may be aggravated by exposure to sunlight or by stooping. It gradually clears unless perpetuated by emotional cause. It may be associated with failure of concentration, backache, insomnia, depression, postural dizziness, functional ocular symptoms, muscular limb pains, effort symptoms, poor memory, dreams, dyspepsia and vertigo. In some cases there is a change in personality from agreeableness to chronic irritability.

> "Many of these symptoms are frankly hysterical in nature, and they are strikingly correlated with predisposition to psychoneurosis, as determined by psychiatric study of the personality. They are only partially correlated with the severity of the acute illness" (Ballard and Miller 1945).

My experience is in agreement with this judgment. These sequelæ are nearly all temporary and disappear within a year or two. Maddock (1943) and Degen (1945) each reported on the after-histories of about 1000 patients discharged from hospital during the war. These patients were visited by nurses, and the symptoms complained of were recorded. In Maddock's series 51 patients recorded as having complaints were ex-patients of the Park Hospital. These were requested to attend for medical examination, and 34 of them did so from some nine months to two and a half years after discharge from the hospital. Of the 34, no sequelæ could at that time be detected in 16, and in a further 7 cases the sequelæ reported were due to causes unconnected with the meningitis. In 2 cases the complaints were "backache" and "weakness of ankle" and appeared to be clearing. Of the remaining 9 cases 8 were deafness and 1 loss of an eye—all certainly due to the meningitis. This small experience fits in with other observations that, within a year or two of the attack of the disease, functional sequelæ have nearly all cleared, and that in well-treated cases there is little residual disability except deafness. However, it was found in both world wars that suggestion by doctors and others plays a significant part in the production and perpetuation of the psychiatric group of sequelæ, and that admission to hospital must for this reason be avoided.

The principal complications in my 706 cases were as follows:

Complication	*No. of cases*
Deafness	33 (4·6%)
Arthritis, bursitis, tenosynovitis	33 (4·6%)
Lower-motor-neurone paresis:	
III nerve	4 (0·6%)
IV ,,	1 (0·2%)
VI ,,	20 (2·8%)
VII ,,	11 (1·5%)
Upper-motor-neurone paresis: VII nerve	5 (0·7%)
Spastic paralysis, jacksonian convulsions	7 (1·0%)
Hemiplegia	3 (0·4%)
Thrombosis of superior longitudinal sinus	1 (0·2%)
Iridochoroiditis	2 (0·3%)
Panophthalmitis	1 (0·2%)
Auricular fibrillation	3 (0·4%)
Glycosuria (non-diabetic)	5 (0·7%)
Bronchopneumonia	4 (0·6%)
Empyema	1 (0·2%)
Hydrocephalus, arachnoiditis	10 (1·4%)
Herpes febrilis (extensive)	10 (1·4%)
Relapse	3 (0·4%)
Second attacks	4 (0·6%)

Treatment of Ordinary Form

CHEMOTHERAPY

In the ordinary form of the disease the infection is best combated with sulphonamides alone. Penicillin is not required either systemically or intrathecally. Several controlled series have shown that penicillin is inferior to sulphonamides in the treatment of the ordinary form (*Lancet* 1947). The best drugs in my experience are sulphathiazole and sulphadiazine. Some have claimed that sulphanilamide is equally good. I had extensive experience with this drug in 1937 and 1938 and learnt that low dosage with sulphanilamide is much more dangerous than it is with the newer drugs. I have never seen drug-resistant meningococci except where sulphanilamide was used. Moreover, this drug often causes cyanosis and mental confusion. Sulphanilamide should be used when renal blockage is feared (its acetyl derivative is much more soluble in urine than that of other sulphonamides) and either it or 'Sulphamezathine' in congestive heart-failure when adequate fluids cannot be given. A theoretical objection to sulphathiazole, still held in some quarters, is its low concentration in the C.S.F.—15–40% of the blood-level. Many cases in my series, treated with rapid and complete success, had only about 1 mg. per

Digitized by Google

100 ml. of free sulphathiazole in the C.S.F. during the first three days of treatment and about half this concentration thereafter. Such low concentrations were never ineffective, provided the patient was not moribund or beyond the reach of drugs.

The scale of dosage used throughout the series was that recommended by the Medical Research Council (1943) which is now standard practice in most British hospitals. Important points are that the dosage for infants of any age over 2 months during the first three or four days of treatment should never be less than 3 g. daily, and for adults 9 g. daily. It is well to begin with a "loading" intravenous dose in all severe cases. The best drug for intravenous or intramuscular injection is 'Soluthiazole' (M. & B.), which is nearly neutral (about pH7) but not quite isotonic. It is unirritating and has completely superseded the highly alkaline sodium salts. Sulphathiazole or sulphadiazine by mouth should always be given in an alkaline mixture containing the equivalent of gr. 20 each of sodium citrate and sodium bicarbonate to keep the urine alkaline, and at least 5 pints of fluids for an adult should be given daily.

OTHER TREATMENT

Spinal drainage, other than that obtained by the first lumbar puncture, is rarely necessary. The C.S.F. is nearly always sterile twelve to forty-eight hours after efficient sulphonamide therapy has been begun, and, with the infection overcome, the pressure rapidly becomes normal.

Sedation.—It is well to avoid morphine even in violent delirium since, among other undesirable effects, it increases the tendency to retention of urine and so to the deposition of crystals in the renal tubules and pelvis. 'Sodium amytal' gr. 3 combined with paraldehyde min. 120 is a good sedative hypnotic. Paraldehyde alone is seldom effective, unless as much as 6 drachms is given to an adult. A useful barbiturate sedative-hypnotic is 'Somnifaine' (Roche), of which repeated doses of 2 ml. may be given intramuscularly or by mouth.

Restraint.—A bed with cot sides is most useful for delirious patients. Restlessness and getting out of bed by unconscious patients is often due to a desire to urinate. This should be anticipated.

Urinary Tract.—If there is retention of urine, the catheter should be used before the bladder is greatly overdistended. If retention persists, a self-retaining catheter should be passed, or an ordinary one tied in for a few days. The chemotherapy will usually control catheter infection, provided reasonable aseptic precautions are taken. Hæmaturia or oliguria is rare when sulphonamides are given with alkali; but, if they appear, the drug must be promptly changed or stopped, and warmth or diathermy applied to the loins. Fluids must be pushed, unless there is threatened anuria, which should be promptly treated by ureteric catheterisation and wash-out.

Glycosuria may be ignored, unless it is due to diabetes, when the insulin intake must be regulated.

Concurrent pneumonia is not uncommon in infants and is very serious. The oxygen tent is very helpful in such cases.

Special Syndromes

FULMINATING SEPTICÆMIA OF ADRENAL AND MIXED TYPES

This is a medical emergency requiring immediate multiple measures.

(*a*) Combat the infection with sulphathiazole or sulphadiazine combined with systemic penicillin in high dosage.

(*b*) Combat shock by adrenal replacement therapy, especially adrenal cortical extract—e.g., 'Eucortone' 5 ml. intramuscularly or more every four hours; plasma intravenously seems also to be indicated in the present state of our knowledge.

(*c*) Combat anoxæmia with oxygen, especially the oxygen tent for a child.

(*d*) Combat any special complications—e.g., hyperglycæmia, with insulin, dehydration with salines, &c.

Combating the infection is the most important measure. Both adrenal replacement and plasma for shock symptoms should at present be used, though the exact value of each cannot easily be assessed.

It is of the utmost importance to establish the diagnosis of the syndrome early by careful examination, including blood-pressure readings, and then to initiate full treatment without delay. A fair proportion of lives can be saved, at least in the pure adrenal type. In the mixed type the same measures are applicable, but, in addition, 20 ml. or more of 50% glucose may be injected intravenously in an attempt to relieve the œdema of the brain and the intracranial pressure.

FULMINATING SEPTICÆMIA OF ENCEPHALITIC TYPE

(*a*) Combat the infection with intravenous and intramuscular soluthiazole and penicillin.

(*b*) Feed the patient by nasal tube.

(*c*) Combat dehydration with parenteral or rectal saline.

(*d*) Combat the œdema of the brain with intravenous hypertonic glucose.

ACUTE DIFFUSE ENCEPHALITIC SYNDROME

(*a*) Combat the infection with intravenous and intramuscular soluthiazole and penicillin until consciousness is restored, and thereafter with sulphonamides by mouth.

(*b*) Feed the patient by nasal tube.

(*c*) Correct dehydration.

(*d*) Give 20 ml. of 50% glucose intravenously to reduce œdema of the brain, and repeat as necessary.

This last measure is sometimes dramatically successful in this syndrome, but sometimes it appears to have no effect.

A man of 62, after thirty-six hours' deep coma, became conscious within a few minutes of the injection of the hypertonic glucose. The lucid interval lasted only 5 min., after which he relapsed into deep coma within the next half-hour. Repetition of the dose next morning had a similar dramatic effect, but this time he remained conscious and slowly recovered.

CHRONIC FORM

Hydrocephalus.—Ventricular drainage by puncture should be tried, but it is rarely successful in re-establishing the flow of C.S.F. In infants and young children hydrocephalus sometimes clears spontaneously after some months, even when temporary blindness seems to have been present. If the condition has not cleared in six months and the head is enlarging, neurosurgery may possibly be able to re-establish drainage, not without considerable operative risk. In one of my cases the anterior wall of the third ventricle was removed to provide an outlet for the retained fluid to flow over the surface of the brain in the subdural space. No permanent benefit, however, resulted from this operation. I am indebted to Mr. Dickson Wright for information on Hyndman's operation (ventriculocisternostomy) which appears to be promising. A communication can be made from ventricle to subarachnoid space by disrupting the pia-arachnoid and ependyma of the choroid plexus. This provides an effective means of shunting the circulation of the fluid from the ventricle through the subarachnoid spaces of the tela choroidea to the basal cisterns, which, fortunately, are rarely obliterated by the chronic inflammatory process (Hyndman 1946).

Paraplegia.—Where there is compression paraplegia, neurosurgeons have had a few successes with an extensive laminectomy and freeing of the adhesions. In the

Digitized by Google

following case, however, only temporary improvement was obtained.

A woman of 31 was admitted on the fifteenth day of disease with a fortnight's history of intermittent headache, backache, vomiting, and slight stiffness of the neck, during most of which time she had been ambulant. The relatively mild symptoms had misled the doctor in attendance, and the diagnosis of meningitis was overlooked.

On admission she was conscious and rational, with pyrexia, rigid neck, slight upper-neurone left facial paresis, unequal pupils, transient diplopia, right knee-jerk diminished, fundi normal, C.S.F. scanty, xanthochromic, cells 309 per c.mm. (mononuclears 70%), chlorides 590, *protein* 1150 *mg. per* 100 *ml.* Colloidal gold early mid-zone curve; Wassermann reaction weak positive (negative in blood); a few meningococci seen in films but none cultured. Complement-fixation test for meningococcal infection positive (Dr. R. Cruickshank) white-cell count 14,600 per.c.mm. (polymorphs 84%).

Treatment.—Sulphathiazole 9 g. daily, gradually reduced to 4 g. daily, for eight days.

Course.—Patient improved gradually but had severe chronic headache in left frontal region for many weeks, with vomiting at times. Lumbar puncture on several occasions produced only a few ml. of xanthochromic and highly proteinous sterile C.S.F., and after three months no fluid. Cisternal puncture gave a dry tap on two occasions. Ventricular puncture after three months gave a clear fluid from each ventricle at normal pressure, but this did not relieve headache at once. Headache spontaneously cleared, however, seven days after the second ventricular puncture, three and a half months after admission. Three weeks later, spastic paraplegia with some sensation loss in right leg. Six weeks later, spastic paraplegia in both legs, feeling of a band round waist, tickle sensation in this region lost, pinprick and vibration sense lost in both limbs. Diagnosed as compression paraplegia from D5 to D12.

Operation (Mr. Dickson Wright).—Cisternal puncture having at this time yielded fluid, laminectomy from D3 to D12 was done, and adhesions were freed. As a result patient could move her legs, but recovery was incomplete. Cisternal 'Lipiodol' now revealed lower limit of fluid to be C2 vertebra. After injection of lipiodol, left frontal headache and vomiting returned, and many ventricular punctures revealed a return of her hydrocephalus and did not relieve it.

Second Operation.—Foramen of Majendie found completely closed with thin diaphonous adhesions; double hydrocephalus. Foramen was cleared. Four days after the second operation patient died of œdema of medulla. Though the neurological signs pointed to obstruction at about D5, there were dense adhesions from C2 to D12, as well as in the posterior fossa at the foramen of Majendie.

PROPHYLAXIS

Meningococcal infection is endemic in most countries. It never dies out completely but persists to a variable extent in the nasopharynx of carriers, and in abortive, mild, and other cases at all times. It cannot therefore be eliminated by the isolation of clinical cases. Nevertheless, with few exceptions, patients with clinical meningococcosis should be removed to hospital for confirmation of diagnosis and effective treatment. Prophylaxis among large bodies of colonial troops by injection of meningococcal vaccines was tried in presulphonamide days without convincing success, and a skin test for immunity was also in the experimental stage. These measures have been superseded by mass prophylaxis with sulphonamides.

Carriers.—The complexity of the carrier state was demonstrated by investigations in the great semi-isolated U.S.A. military camps during the war. Phair et al. (1944) showed, in one infected camp, that when swabs from 100 soldiers were cultured on multiple plates at intervals during ten weeks, 91% were found positive at one time or another, more than half of them harbouring two or more specific strains. It is now clear that the carrier-rate of a group cannot be adequately determined by single cultures, and that the carrier state of a group is a complex ever changing pattern. It is therefore a vain endeavour to attempt to isolate carriers.

Mass prophylaxis by administration of sulphonamide simultaneously to all members of an infected semi-isolated group does eliminate carriers as well as clinical cases to a very large extent. This method has been used with success to break an epidemic in such semi-closed communities as (1) a children's residential home (Meehan and Merrilees 1940); (2) large military camps (Painton 1944); and even (3) a city of 100,000 inhabitants set in mountainous surroundings. There is evidence that a single dose of sulphadiazine 2 g. (or its equivalent) given simultaneously to every member of the selected community will achieve this purpose (Phair et al. 1944). The carrier-rate is reduced to a very low figure—e.g., 5–10%—for three weeks or more and then gradually rises, but by the time it does so the occurrence of clinical cases has stopped. This method has little application, however, to the infected individual household of an ordinary civilian community, since its members, unless isolated from the rest of the community, would quickly become reinfected.

Quarantine of contacts is useless and an unnecessary waste of time. Prophylactic sprays and douches are also useless and may be harmful. Fomites, unless very recently contaminated, do not convey the infection.

The convalescent patient now rarely harbours meningococci, since the sulphonamide treatment destroys them. The practice of swabbing his nasopharynx before release from hospital has been generally discontinued as not worth while.

The routine use of masks by attendants on patients in the acute stage is generally impracticable and is unnecessary, since direct infection is extremely rare. Their occasional use for a short time is advisable when an attendant is exposed to gross infection—e.g., in struggling with a delirious patient.

It is a great pleasure to acknowledge the valuable assistance I have received from many past and present members of the medical and nursing staff of Park Hospital, and of the medical and technical staff of the Southern Group Laboratory.

REFERENCES

Allison, V. D. (1947) personal communication.
Baker, A. B. (1935) *Amer. J. Path.* **11**, 185.
Ballard, S. I., Miller, H. G. (1945) *Lancet*, ii, 273.
Banks, H. S., McCartney, J. E. (1942) *Ibid*, i, 219.
— — (1943) *Ibid*, i, 771.
Beeson, P. B., Westerman, E. (1943) *Brit. med. J.* i, 497.
Brick, I. B. (1948) *New Engl. J. Med.* **238**, 289.
Crawford, C. (1944) *Brit. med. J.* i, 325.
Degen, J. A. jun. (1945) *Ibid*, ii, 243.
Ebert, R. V., Stead, E. A. jun. (1941) *J. clin. invest.* **20**, 671.
Fairbrother, R. W. (1947) *J. clin. Path.* **1**, 10.
Flack, M. (1917) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 3. (Studies in Cerebrospinal Fever.)
Gordon, W. H., Shimkin, M. B. (1943) *J. Amer. med. Ass.* **123**, 147.
Harries, G. E. (1942) *Brit. med. J.* ii, 423.
Holm, M. L., Davison, W.C. (1919) *Bull. Johns Hopk. Hosp.* **30**, 324.
Hyndman, O. R. (1946) *J. Neurosurg.* **3**, 426.
Joe, A. (1942) *Edinb. med. J.* **49**, 628.
Kinsman, J. M., d'Alonzo, C. A., Russi, S. (1946) *Arch. intern. Med.* **78**, 139.
Lancet (1947) ii, 514.
Maddock, E. C. E. (1943) *Mon. Bull. Min. Hlth*, **2**, 111.
Medical Research Council (1943) War Memorandum no. 10.
Meehan, J. F., Merrilees, C. R. (1940) *Med. J. Aust.* ii, 84.
Morison, J. E. (1943) *Lancet*, i, 800.
Painton, J. F. (1944) *Milit. Surg.* **95**, 267.
Phair, J. J., Schoenbach, E. B., Root, C. M. (1944) *Amer. J. Publ. Hlth*, **34**, 148.
Priest, R. (1947) *J. R. Army med. Cps.* **89**, 1.
Rich, A. R. (1944) *Bull. Johns Hopk. Hosp.* **74**, 1.
Roberg, N. B. (1945) *Bull. U.S. Army med. Dept.* **4**, 97.
Rolleston, H. (1919) *Lancet*, i, 541.
Shuttleworth, F. N. Benstead, J. G. (1947) *Brit. med. J.* ii, 568.
Thomas, H. M. jun. (1943) *J. Amer. med. Ass.* **123**, 264.
Van Rooyen, C. E., Morris, J. C. (1941) *J. R. Army med. Cps*, **76**, 200.
Wartman, W. B., Hanger, I. C. (1944) *Amer. J. med. Sci.* **208**, 234.
Williams, H. (1942) *Med. J. Aust.* ii, 557.

Digitized by Google

INFECTION THROUGH SOAKED DRESSINGS

LEONARD COLEBROOK
M.B. Lond., F.R.C.O.G., F.R.S.
MEMBER OF SCIENTIFIC STAFF, MEDICAL RESEARCH COUNCIL

A. M. HOOD
TECHNICIAN

From the Medical Research Council Burns Unit, Birmingham Accident Hospital

IN 1943 Owens, in a paper on the use of pressure dressings in the treatment of burns and other wounds, reported that "outside contamination can reach a wound through the entire thickness of a dressing." That conclusion was based on in-vitro experiments with artificial "wounds" which showed that "it was possible to draw organisms through as many as 64 thicknesses of gauze from the outside." Other experiments showed that a layer of 'Cellophane' interposed between the moistened dressings and the contaminant effectively barred the passage of the organisms. (It may well be that this passage of organisms through a dressing from the outside was recognised during the Listerian era, and that the impregnation of the dressing-materials with antiseptics —e.g., mercuric cyanide—was partly designed to prevent it, but we are not familiar with any experimental work on the subject.)

Owens's work did not come to our notice until 1947, after we had carried out similar in-vitro experiments which are briefly reported here. We became interested in the subject in the following circumstances:

A.B., a man with severe electric burns of both hands and forearms, received the standard plenary dressing within two hours of his accident. Swabs from the hands were examined before they were cleaned and did not grow *Ps. pyocyanea* or any other pathogen. The plenary dressing consisted of thorough cleaning with cetrimide ('Cetavlon') solution, a generous application of cream containing penicillin 200 units per g. and sulphathiazole 3%, and then plenty of sterile gauze and wool, the whole carefully fixed with many crêpe bandages under mild pressure, completely enclosing both limbs to well above the burned areas. This dressing was done under very strict aseptic precaution in the room used exclusively for the first dressing of fresh burns. During the previous twelve months there had been no instance of infection of a fresh burn referable to infection in this room.

As often happens with severe burns, the dressings and bandages over the dependent parts became soaked with serous exudate, and according to custom these dressings were "packed" with more sterile wool and more crêpe bandages. The original dressings were not disturbed in any way, because they were in good order and fitting snugly to the limbs. On the fifth day the characteristic blue-green staining of *Ps. pyocyanea* was noticed on the outer bandage of one arm. Re-dressing next day revealed the presence of *Ps. pyocyanea* on both hands.

Reflection on the possible source of this infection suggested at once a connexion with two other men in the same ward (one only 12–15 ft. away) with a similar infection. Both of these had old burns already infected on admission (4 months in one case and 14 days in the other). They were confined to bed, but there was clearly the possibility that the organisms had been transmitted from them to A.B. either by the air or by indirect contact —e.g., by nurses' hands or clothing during the process of making beds. That at once suggested the question: could the *Ps. pyocyanea* grow through the intact dressings of A.B. when they were soaked with serous exudate?

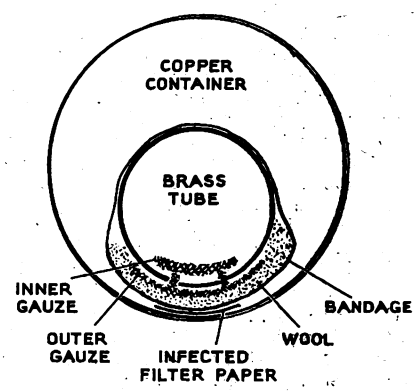
EXPERIMENTS

To investigate this possibility an experimental "wound" was devised and used as follows:

Several holes were drilled near one end of a piece of brass tubing 8 in. long and 2 in. in diameter. Through these holes wicks of gauze were carried to assist the seepage of fluid from a loose piece of gauze placed on the inside of the tube (simulating the "weeping" tissues of a wound) to the gauze, wool, and bandages wrapped round the outside (see figure). The tubing with its "wound" was then placed horizontally, resting on a piece of filter paper (which would later receive the inoculum of organisms), inside a sealed copper container and sterilised in the autoclave.

For each experiment an artificial "wound" of this kind in its container was placed horizontally in the incubator, and the inner gauze was first primed by a series of additions of sterile fluid until, after a few hours, the outer bandage was just moist. Since blister fluid from burned patients was not available in sufficient quantity, the fluid used for most of the tests was dried plasma dissolved in nutrient broth—to simulate the exudate from burned surfaces.

As soon as the outer bandage had become moist (the filter paper helped to detect this), its sterility, as well as that of the inner gauze, was checked by the usual swab examination, and the bandage was then infected by pipetting about 1 ml. of a thousandfold diluted culture of *Ps. pyocyanea* or other organism on to the filter paper. The whole was then reincubated on its side, and further bacteriological tests were made at intervals, both from the inner gauze and from the bandage. If necessary, fresh supplies of sterile fluid were added to the inner gauze from time to time to keep it moist, with appropriate precautions against introducing any infection.



Apparatus used in experiment described in text.

RESULTS

The results were briefly as follows:

Organism and number of strains tested	*Interval between infection of outer bandage and recovery of the organism from inner gauze*
Ps. pyocyanea (9)	Varied from 4 to 48 hr.
Proteus (4)	,, ,, 18 to 42 ,,
Staph. aureus (4)	42 hr.
Diphtheroid bacillus (1) ..	42 hr.
Hæmolytic streptococcus (3)* ..	Varied from 24 to 48 hr.
Coliform bacillus (1)	42 hr.

* For these tests it was necessary to use a silver-plated tube in an aluminium container, because the copper and brass killed the organisms.

Other tests showed:

(1) That a plaster-of-paris shell over the bandage did not interfere with the ingrowing of the organisms. (*Ps. pyocyanea* grew through in 86–110 hours, and *Proteus* in 42 hours.)

(2) A sheet of cellophane (supplied by British Cellophane Co. with the designation P.T.300) interposed between the wool and the bandages did not allow the passage of organisms (6 tests).

(3) A thin sheet of 'Polythene' was also an effective barrier.

(4) When the outermost layer of plasma-soaked dressing consisted of many layers of mercuric-cyanide gauze, *Ps. pyocyanea* and *Proteus* and *Staph. aureus* grew through, but not hæmolytic streptococcus, which seemed to be killed off by the cyanide.

Digitized by Google

DISCUSSION

It is therefore clear, nor is it surprising, that organisms can readily grow through a dressing steeped in plasma plus broth, and it seems a safe assumption that the same will happen if the nutrient fluid is the normal exudate from a burned surface, since small inocula of these same organisms—hæmolytic streptococcus, staphylococcus, *Proteus*, and *Ps. pyocyanea*—have been found to grow freely in such exudate (blister fluid).

How often such an ingrowth of organisms does in fact occur through dressings soaked in vivo with serous exudate or blood we do not know. It will always be difficult to prove. It probably happened in the case of A.B., and it may well have been responsible for a number of other added infections by *Ps. pyocyanea* which developed between the first and second dressings of fresh burns (the period of maximal exudation) during the latter part of 1947 (Colebrook et al. 1948). It may also have been responsible for many of the early infections of burns by hæmolytic streptococci reported by Cruickshank (1935) from the burns wards of the Glasgow Royal Infirmary and noted by Stuart in the same wards during 1941 (see Colebrook et al. 1945). In a ward with many other infections by that organism (from which it may be disseminated by the air) the passage of hæmolytic streptococci through intact but soaked dressings would be particularly liable to occur because of the readiness with which it can multiply in fresh wound exudate from the smallest implant (Wright 1915, Wright et al. 1918).

Quite apart from burns, the tendency for dressings to become soaked after operations is well known to surgeons and ward sisters. The possibility of growth of organisms through such dressings should always be borne in mind.

The best way to prevent it is not yet clear. Insertion of a thin plastic sheet under the outer bandage should be effective in many cases, but the use of some of these materials has certain disadvantages. Cellophane, for instance, is difficult to apply because of its inelasticity and its liability to tear; the bandages over it also tend to slip on the smooth surface. Other plastic films with better mechanical properties, such as polythene, are impervious to water vapour as well as to water; and, if the dressing is completely enclosed by them and is bandaged firmly to the skin all round, the underlying wound becomes sodden and healing may be retarded. The ideal material, besides being flexible and strong, would be pervious to water vapour but not to liquids or to bacteria. Such a material (a derivative of 'Nylon') has already been produced in small quantities, and some experimental results obtained with it have been described by Bull et al. (1948). It is hoped that larger quantities of this plastic will soon be available for more extended trials.

SUMMARY

The possibility that wound pathogens can readily "grow through" an intact dressing when this becomes soaked with exudates has been investigated.

A model wound was constructed and covered with the usual gauze, wool, and bandages. After repeated instillation of sterile serous fluid into the wound till the outer bandage was just moist, *Ps. pyocyanea* or other wound pathogens were brought into contact with the outer bandage and the whole was incubated. Motile organisms such as *Ps. pyocyanea* and *Proteus* invariably passed through to the "wound" within a few hours; hæmolytic streptococci and staphylococci passed through a little more slowly.

It is suggested that some of the hospital cross-infections of burns and scalds (which frequently weep copiously during the first few days), and probably also of other open wounds whose dressings become soaked, may arise in this way.

A sheet of cellophane inserted in the dressing prevents the ingrowth of organisms, but is not the ideal barrier. A flexible and strong plastic film which is pervious to water vapour but impervious to bacteria is under trial.

REFERENCES

Bull, J. P., Squire, J. R., Topley, E. (1948) *Lancet*, ii, 213.
Colebrook, L., Gibson, T., Todd, J. P., Clark, A. M., Brown, A., Anderson, A. B., Semeonoff, E. (1945) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 249.
— Duncan, J. M., Ross, W. P. D. (1948) *Lancet*, i, 893.
Cruickshank, R. (1935) *J. Path. Bact.* 41, 367.
Owens, N. (1943) *Surg. Clin. N. Amer.* 23, 1354.
Wright, A. E. (1915) *Brit. med. J.* i, 625.
— Fleming, A., Colebrook, L. (1918) *Lancet*, i, 831.

A METHOD OF TESTING ANALGESICS IN MAN

A. J. H. HEWER, M.B. Lond., D.A.
RESEARCH ANÆSTHETIST
C. A. KEELE, M.D. Lond., F.R.C.P.
LECTURER IN PHARMACOLOGY
MIDDLESEX HOSPITAL MEDICAL SCHOOL, LONDON

THE usual methods of testing analgesics are based on measurements of the threshold intensity of some stimulus required to elicit pain; but analgesics are mostly used to relieve existing pain. Since the presence of pain may greatly reduce the threshold-raising action of such drugs (Hardy et al. 1940), measurements of thresholds may not correlate with the ability of a drug to relieve pain associated with disease. Further, such drugs might act differently on superficial pain (produced in most threshold studies) than in deep pain.

We have tested the power of analgesics to relieve pain experimentally induced by the contraction of ischæmic muscles. Harrison and Bigelow (1943) noted the effects of analgesics on the number of ischæmic muscular contractions required to produce pain, but we have tested the effectiveness of these drugs in the relief of existent pain of ischæmic origin. Our method (Hewer and Keele 1947) therefore lies somewhere between the usual threshold studies and clinical observations on the effectiveness of analgesics. It is illustrated by tests on different groups of analgesics.

Four normal persons were the subjects of our experiments: two medical students (R. M. L. D., aged 20, and J. W. M., aged 19) and ourselves (aged 27 and 41). The tests were usually performed in the late afternoon, with the subject lying quietly on a couch.

PRODUCTION OF ISCHÆMIC MUSCLE PAIN

After a preliminary rest of 5–10 min. a sphygmomanometer cuff was applied to the upper arm and inflated rapidly to 220–230 mm. Hg to cut off the circulation to the arm distal to the cuff. The hand and forearm muscles were next exercised by rhythmically compressing a disconnected sphygmomanometer bulb (to provide a constant resistance against each contraction). After 30–45 such contractions an aching pain usually developed in the flexor muscles in the forearm, and sometimes also in the muscles of the hand. When 50–60 contractions had been completed, there was slight or moderate pain in the forearm muscles. The contractions were then stopped, and the arm was rested with the ischæmia still maintained. At first the pain present decreased, sometimes to zero, and tingling was felt. After 1–3 min., with the arm still at rest, the pain returned and began to build up steadily, until after 8–15 min. (the speed of development of the pain depending on the number of contractions, room temperature, and perhaps other factors) the pain became intolerable. The cuff was then deflated, and the pain disappeared within a few seconds.

At first it was easy to distinguish 5 grades of pain: slight, moderate, severe, very severe, and intolerable. With further experience it was easy to distinguish intermediate grades of intensity of pain, and for convenience the pain intensity has been described in units from 1 to 10.

Digitized by Google

TESTS OF ANALGESICS

In testing the effects of analgesics the pain was allowed to reach a value of 4–5 units. The drug to be tested was then administered—gases by inhalation, and other drugs by intravenous injection.

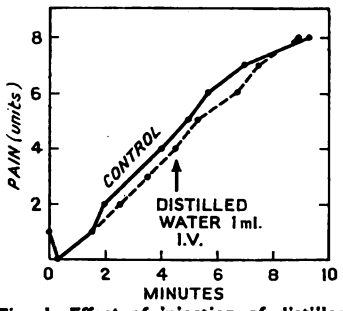


Fig. 1—Effect of injection of distilled water on ischæmic muscular pain in forearm after 55 contractions in subject J. W. M. compared with increase of pain without any injection. Note similarity of curves.

The gases studied were nitrous oxide and cyclopropane. Nitrous oxide was given in concentrations of 10–40% in oxygen, and cyclopropane in concentrations of 2–3% in oxygen. The proportions of the gases in oxygen were measured with a 'Rotameter,' and the rate of flow was kept fast enough to prevent rebreathing.

The analgesics given by intravenous injection were as follows:

(1) Morphine (sulphate or hydrochloride).
(2) Pethidine hydrochloride.
(3) *dl*-2-dimethylamino-4 : 4-diphenyl-heptan-5-one hydrochloride ('Physeptone,' 'Amidone,' 'Miadone,' 'Hoechst 10820').
(4) *dl*-1-dimethylamino-3 : 3-diphenyl-hexan-4-one hydrochloride ('Hoechst 10582').
(5) *dl*-2-dimethylaminomethyl-3 : 3-diphenyl-hexan-4-one hydrochloride ('Isoamidone').
(6) *dl*-2-l'morpholino-4 : 4-diphenyl-heptan-5-one hydrochloride ('C.B.11').
(7) Procaine hydrochloride.
(8) Thiopentone soluble.
(9) 'Benadryl' hydrochloride.
(10) N-p-methoxybenzyl-N-dimethylaminoethyl-2-aminopyridine maleate ('Neoantergan,' 'Anthisan,' pyranisamine maleate).
(11) N-phenyl-N-benzyl-2-methylimidazoline ('Antistin').
(12) Tetraethylammonium bromide (T.E.A.B.).

When morphine, pethidine, and physeptone were given in larger doses, the rate of intravenous injection was 5 mg. per min. for morphine and physeptone, and 50 mg. per min. for pethidine. The maximal doses of morphine, physeptone, and pethidine were 7·5 mg., 7·5 mg., and 75·0 mg. respectively. When the duration of injection was varied with the dose, the needle was kept in the vein for the maximal period of $1^1/_2$ min., so that the subject could not guess the size of the injected dose from the duration of its administration. Later on, when threshold studies were undertaken, the period of injection was 1 min. in all cases.

CONTROL OBSERVATIONS

In studies based on subjective impressions adequate control observations are imperative. Therefore (1) we obtained numerous records of the increase in pain with time in the absence of any injection; (2) we sometimes injected distilled water; and (3) in determining threshold doses we injected subliminal quantities of analgesics, the subject being unaware of the nature or the dose of the injected drug. In all these instances there was a steady increase in intensity of pain to a value of 8 units in 8–15 min. Under the conditions of our experiments there were some minor fluctuations in the ischæmic pain, but these were in no way comparable with the clear-cut relief of pain produced by an adequate dose of an analgesic.

Fig. 1 illustrates the absence of effect of an injection of distilled water in a subject (J. W. M.) who was expecting an injection of an effective dose of pethidine and was extremely disappointed with his inability to record any analgesia. The rate of increase in pain intensity after distilled water is compared with a typical rate of increase in the absence of an injection; the curves are clearly very similar.

Fig. 2 shows curves obtained from subjects R. M. L. D. and C. A. K. when they received subliminal doses of physeptone (0·25 mg.) and C.B.11 (0·20 mg.) respectively. In both cases the rate of increase in pain intensity was similar to that recorded when no injection was given.

RESULTS OF INJECTION OF ANALGESICS

Intravenous injection of morphine, pethidine, physeptone, or C.B.11 produced effects which developed either during the latter part of the injection or 1 or 2 min. after the injection. The effects rapidly became maximal with the larger doses—e.g., 5·0–7·5 mg. of morphine or of physeptone, and 50–75 mg. of pethidine—and the relief of pain was associated with well-marked side-effects (see below).

A typical illustration of the analgesic action is seen in fig. 3, which shows the effect of 5 mg. of physeptone injected in 1 min. in subject J. W. M. The relief of pain was complete; but the effect was transient, and subsequently the pain increased rapidly. The brief duration of the analgesia was due partly to the fact that the intensity of the ischæmic muscle pain was increasing continuously and soon overcame the initial maximal effect of the intravenous analgesic, and partly to redistribution of the drug from its original site of fixation in the brain. With smaller doses the relief of pain was proportionately less.

At first we tried to compare the analgesic potencies by finding the smallest dose which would produce complete relief of pain of 4–5 units intensity, as shown, for example, for subject J. W. M. with physeptone (fig. 3). This method of comparison suggested that 7·5 mg. of morphine was equivalent to 7·5 mg. of physeptone and to 75·0 mg. of pethidine; in other words, morphine and physeptone were equianalgesic, and both were about 10 times as potent as pethidine. However, such large doses produced side-effects which were too great, and after effects which were too protracted, for the necessary repeated observations. So we finally decided to determine the threshold dose of each drug—i.e., the smallest dose which would produce a definite effect on 4–5 units of pain. Such tests were found most satisfactory and had the great advantage of causing little general disturbance and no after effects, with the result that several tests could be made in a week. Over short periods—e.g., a few weeks—the threshold values remained constant; but, when tests were repeated after several months, changes in threshold doses were found (see below).

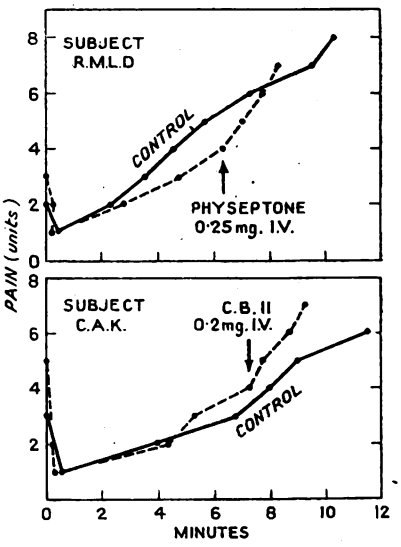


Fig. 2—Effects of injections of subliminal doses of analgesics on ischæmic muscular pain in forearm (55 contractions in subject R. M. L. D. and 50 contractions in subject C. A. K.) compared with increase of pain without any injection. Note similarity of curves.

DETERMINATION OF THRESHOLD DOSE

The threshold dose for each drug was determined as follows:

Doses well above and well below the threshold were given. Next the range was narrowed till there was only a small difference between the effective and ineffective doses. During

Digitized by Google

this period of testing, the response to a previously determined threshold dose of another drug was usually retested to check the subject's sensitivity.

For example, with subject C. A. K. 0·2 mg. of C.B.11 had no effect, but 0·3 mg. reduced the pain intensity from 4 to 2 units. The threshold dose was taken as 0·25 mg. In other instances the subject's response was of a border-line character, a sort of plateau effect in which the pain curve was just affected. The dose which produced such a response was accepted as the threshold value.

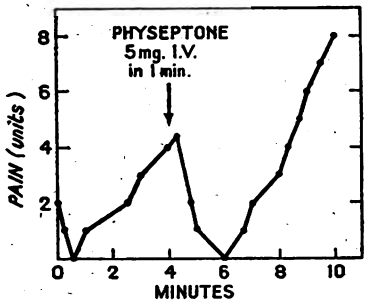


Fig. 3—Analgesic action of physeptone on ischæmic muscular pain in forearm (55 contractions) in subject J. W. M.

Threshold determinations gave different results in the three persons studied. The threshold doses found for several drugs were as follows:

Drug	C. A. K.	J. W. M.	R. M. L. D.
Morphine	0·002 mg.	0·1 mg.	0·35 mg.
Pethidine	7·5 mg.	1 mg.	7·5 mg.
Physeptone	0·25 mg.	0·1 mg.	0·3 mg.
C.B.11	0·25 mg.	0·01 mg.	0·4 mg.
Isoamidone	0·3 mg.	—	—
Hoechst 10582 ..	0·4 mg.	—	—

Thus in subject C. A. K. physeptone and C.B.11 were both 30 times as potent as pethidine (the action of morphine was exceptional in this person and is discussed below). In subject J. W. M. morphine and physeptone were both 10 times as potent as pethidine, but were only $^1/_{10}$ as powerful as C.B.11. In subject R. M. L. D. morphine, physeptone, and C.B.11 were about equianalgesic and were 20–25 times more potent than pethidine.

These results may be compared with the figures obtained by Thorp et al. (1947) in experiments on analgesia in rats, in which morphine and physeptone were equally active and about 10 times as potent as pethidine.

We think that individual variations in sensitivity to analgesics are important. Subject J. W. M. was always more responsive to analgesic drugs than subject R. M. L. D. This difference was seen at all dosage levels but was most clearly shown in the threshold measurements. Subject C. A. K. closely resembled subject R. M. L. D. except in his response to morphine. These differences could hardly be attributed solely to differences in body-weight (J. W. M. weighed 11 st. 1 lb., R. M. L. D. 13 st., and C. A. K. 13 st. 4 lb.).

It is therefore obvious that clinical differences in response to analgesics can, at least in part, be ascribed to differences in sensitivity towards them. Since in our experiments the drugs were given intravenously, the differences in sensitivity cannot be due to variable absorption and must therefore represent true differences in analgesic potency. In patients variable absorption from the gut or from the site of injection will contribute further possibilities for variation in response.

CHANGES IN THRESHOLD WITH TIME

We have already pointed out that the threshold should be determined in a short time. The reason for this precaution is that the threshold may change after several months. It would perhaps be generally expected, from the well-known development of tolerance to morphine, that the threshold would rise with the regular performance of these analgesic tests, but the exact opposite was invariably found.

For example, on June 12, 1947, in subject R. M. L. D. the threshold dose of physeptone was 2·5 mg., whereas on Jan. 7, 1948, it was 0·4 mg. Threshold values were not usually determined in the earlier part of our work; hence precise differences in sensitivity cannot be stated, but the responses to supraliminal doses undoubtedly increased with time. Thus in subject J. W. M. the initial response to 1 mg. of C.B.11 was a reduction of pain from 5 to 2 units; this same response later was given to 0·1 mg. of C.B.11.

In general the increase in sensitivity appeared to be about equal for all the drugs studied, and was probably due, at least in part, to the acquisition of greater skill in recognising small changes in pain intensity, but we feel that some true increase in sensitivity must also have developed.

In subject C. A. K. an extraordinary increase in sensitivity to morphine developed. In May and June, 1947, the effect of 5·0 and 7·5 mg. was to reduce the pain from 4 units to 1 unit and from 4 units to 0 respectively. These doses produced a definite subjective feeling of respiratory depression and a characteristic occipital headache. The reaction was rather unpleasant at first but was followed by euphoria. On Oct. 24, 1947, it was intended to repeat the 5 mg. dose to see how far the response had changed. When only 2·5 mg. of morphine had been given in $^1/_2$ min., the effects developed very suddenly and were much greater in all respects than with 7·5 mg. of morphine five months earlier. Subsequently 0·3 mg. produced an effect definitely greater than did the original 7·5 mg. dose, and later the threshold dose was about 0·002 mg.

Such an increase in sensitivity (about a thousandfold) might suggest an allergic response; but, unlike such a reaction, the hypersensitivity concerned all the pharmacological effects originally elicited by the larger doses. Analgesia, respiratory depression, and occipital headache were about equally intensified. The threshold dose of morphine in J. W. M. was 0·1 mg., and in R. M. L. D. 0·35 mg. The cause of this remarkable sensitisation is not clear, but it might be related to the intravenous route of administration.

ANÆSTHETIC GASES

The analgesic actions of nitrous oxide and cyclopropane were easily demonstrated by the ischæmic-pain method.

Nitrous oxide was given in concentrations of 10-40% in oxygen, the proportions being measured with a rotameter. The ischæmic pain was allowed to develop till the intensity had reached 4 or 5 units, when the gas was inhaled.

A typical result, in subject R. M. L. D., is shown in fig. 4, where inhalation of 20% nitrous oxide and 80% oxygen reduced the pain from 4 units to 1 unit and greatly delayed the increase in pain intensity which would normally have been expected.

In subject J. W. M. the following results were obtained:

Nitrous oxide	Oxygen	Result
10% ..	90% ..	No effect on pain
15% ..	85% ..	Pain fell from 5→3 units
20% ..	80% ..	,, ,, ,, 5→1 unit
30% ..	70% ..	,, ,, ,, 5→1 ,,
40% ..	60% ..	,, ,, ,, 5→0 ,,

Minnitt's apparatus was also tested for its effect on ischæmic muscle pain, 45% nitrous oxide and 55% air

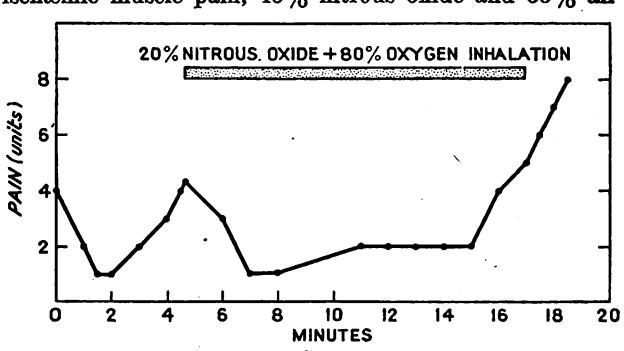


Fig. 4—Analgesic action of nitrous oxide on ischæmic muscular pain in forearm (55 contractions) in subject R. M. L. D.

Digitized by Google

being inhaled. In subject C. A. K. in three separate experiments the pain was reduced from 5 units to 0, 6 units to 0, and 8 units to 1 unit. In A. J. H. H. pain was reduced from 8 to 4 units.

Cyclopropane was studied in a similar way, 2% and 3% cyclopropane in oxygen being given. The results were as follows:

Cyclopropane	*J. W. M.*	*C. A. K.*	*R. M. L. D.*	*A. J. H. H.*
2%	4→2 units	4→1 unit	4→2 units	5→3 units
3%	6→1 unit	4→1 ,,	3→1 unit	6→2 ,,

The effects of both these gases were associated with the usual subjective responses noted during induction of anæsthesia with these agents, the degree of such response being proportional to the concentration of anæsthetic gas. In no case did loss of consciousness result, though 40% nitrous oxide almost produced this effect. These results agree very well with those of Seevers et al. (1937), who observed the analgesic actions of such concentrations of these gases on the response to pinpricks of graded pressure.

INTRAVENOUS PROCAINE

The analgesic actions of intravenous procaine have been described by Lundy (1942), Gordon (1943), Allen (1945), and McLachlin (1945). It has been suggested that procaine administered by this route may act either locally on nerve-endings in regions where increased capillary permeability allows greater escape of procaine from the blood-stream, as might happen in burns, or by an action on the central nervous system probably similar to that of well-known analgesics such as morphine and pethidine.

The ischæmic-pain test shows whether the analgesic action of procaine is central or peripheral. If its intravenous administration relieves this pain, the drug must act somewhere central to the site of arterial occlusion in the upper arm, since none of the drug can penetrate to the site of pain production in the ischæmic muscle.

Procaine has been given intravenously to four persons, the dose being 50 mg. in 1 min., or 100 mg. in 2 min. Analgesia of different degrees was produced in all of eight experiments as follows:

Procaine dose	*C. A. K.*	*J. W. M.*	*R. M. L. D.*	*A. J. H. H.*
50 mg. in 1 min.	4→3 units	5→2 units	—	—
100 mg. in 2 min.	4→0 unit	—	6→2 units	4→0 unit
,, ,, ,,	4→1 ,,	—	—	4→0 ,,
,, ,, ,,	4→1 ,,	—	—	—

There is thus no doubt that intravenous procaine can relieve pain by a central action. This does not exclude the possibility of a peripheral action as well, but the latter component is likely to be very small, since extreme dilution of the procaine will have taken place by the time it reaches the affected part. In our experiments procaine analgesia was accompanied by side-effects such as giddiness, light-headedness, nystagmus, and a sensation of respiratory depression.

THIOPENTONE

Thiopentone has also been shown to exert an analgesic effect on ischæmic muscle pain. Thus 100 mg. of sodium thiopentone injected intravenously in 15 sec. produced relief of pain generally comparable to that produced by 30–40% nitrous oxide. The results in four persons were as follows:

J. W. M.	*R. M. L. D.*	*C. A. K.*	*A. J. H. H.*
4→0 unit	4→1 unit	4→1 unit	4→2 units

None of the persons lost consciousness with this dose, but such side-effects as drowsiness, giddiness, a feeling of remoteness, and confusion were well marked, which may have impaired judgment of the results.

ANTI-HISTAMINE DRUGS

It is well known that the anti-histamine drugs have actions unrelated to their antagonism to histamine. For example, they are mostly more powerful local anæsthetics than procaine, and they have also been claimed to be weak analgesics in rats. We therefore studied the actions of some of these compounds on ischæmic muscle pain. Benadryl, antistin, and neoantergan were given intravenously, and the following threshold doses were found in the two persons tested:

Drug	*C. A. K.*	*R. M. L. D.*
Benadryl	5·0 mg.	5·0 mg.
Antistin	7·5 mg.	12·5 mg.
Neoantergan	2·0 mg.	7·5 mg.

TETRAETHYLAMMONIUM BROMIDE (T.E.A.B.)

The actions of T.E.A.B. have recently been studied in connexion with its ganglionic blocking effects, with particular relation to sympathetic control of vascular tone in the limbs. A patient with causalgia, under the care of Prof. A. Kekwick, showed relief of this pain after intravenous injection of 200 mg. of T.E.A.B. This dose produced a well-marked fall in blood-pressure.

The possibility of a central analgesic action was investigated by injecting T.E.A.B. intravenously into subjects R. M. L. D. (75 mg.) and C. A. K. (100 mg.), when ischæmic pain had been produced in the usual way. Both persons noted slight relief of pain; but, when the doses of T.E.A.B. are compared with the threshold doses of other compounds studied, it will be seen that T.E.A.B. is a very feeble analgesic. However, it may well be that the relief of causalgic pain recorded by Conley et al. (1947) after injection of up to 500 mg. of T.E.A.B. was due more to a central analgesic action than to any circulatory changes.

SIDE-EFFECTS OF ANALGESIC DRUGS

When the larger doses of morphine (5·0–7·5 mg.), pethidine (25–75 mg.), physeptone (2·5–7·5 mg.), or C.B.11 (1·0–2·5 mg.) were given, side-effects were well marked and usually so characteristic that the drug could be readily identified. Apart from differences between the various drugs there were differences between individual responses to the same drug. In studies on threshold doses it was found that with slightly supraliminal doses analgesia could sometimes be obtained without any side-effects.

For example, subject J. W. M. had no side-effects with C.B. 11 in doses less than 0·5 mg., but the threshold analgesic dose was 0·01 mg.; and subject R. M. L. D. had no side-effects with physeptone in doses less than 2·5 mg. (threshold dose 0·3 mg.). On the other hand, subject R. M. L. D. showed side-effects with morphine in doses down to 0·1 mg., but no analgesia with doses less than 0·4 mg.

Thus there was usually analgesia before the onset of side-effects, but sometimes the order was reversed. This might well explain differences in clinical response to analgesics.

The most important side-effect with morphine, pethidine, physeptone, and C.B.11 was euphoria, which lasted for several hours after the larger doses of these drugs. This feeling of well-being usually outlasted other side-effects and in some instances persisted for 24 hours. The four subjects showed differences in their liability to euphoria, the order for the four drugs in each subject being as follows:

C. A. K.: (1) physeptone, (2) pethidine, (3) morphine, (4) C.B.11.

J. W. M.: (1) pethidine, (2) physeptone, (3) morphine, (4) C.B.11.

R. M. L. D.: (1) pethidine, (2) physeptone, (3) morphine, (4) C.B.11.

A. J. H. H.: (1) morphine, (2) pethidine, (3) physeptone, (C.B.11 not tested).

The position of C.B.11 may have been due to the use of small doses of this drug. The differences between other drugs were partly due to accompanying dysphoric effects —e.g., nausea and giddiness, which would easily outweigh any tendency to look on the brighter side of life.

Digitized by Google

The importance of euphoria lies in its close relation to the liability to drug addiction.

The other drugs had different effects on mood. The actions of nitrous oxide were pleasant but differed from those of the drugs just mentioned. The effects of procaine, especially when given by continuous infusion, were described by subjects A. J. H. H. and C. A. K. as definitely unpleasant. There was no euphoria with thiopentone, the anti-histamine drugs, or T.E.A.B.

Other side-effects noted with all the drugs included light-headedness, giddiness, and a feeling of remoteness. With pethidine, physeptone, and procaine nystagmus with blurred and double vision was often noted. Morphine, pethidine, physeptone, C.B.11, and procaine were all liable to produce a sensation of difficulty in breathing. Thiopentone produced confusion and well-marked drowsiness in all subjects. Neoantergan produced drowsiness even in threshold doses with subject C. A. K. but not with subject R. M. L. D.

DISCUSSION

The various methods hitherto used to test analgesics in animals and man have all involved measurement of the threshold of a painful stimulus of brief duration. In man Macht et al. (1916) used a faradic current; Seevers and Pfeiffer (1936) measured the response to graded pressure with von Frey's hairs or needle prick; Hardy et al. (1940) applied radiant heat to the blackened skin of the forehead; Goetzl et al. (1943) applied an alternating current to a dental filling; and Harrison and Bigelow (1943) measured the number of ischæmic muscle contractions in the forearm required to produce pain.

It is plainly an advantage to be able to measure the strength of stimulus, but it must be remembered that analgesics are most often given to patients in whom pain is already present at a level well above threshold. Hardy et al. (1940) have shown that, when morphine is given to persons enduring experimentally induced pain, the pain-threshold-raising action of the drug is almost completely abolished. They suggest that the relief of pain by morphine is due largely to detachment of pain perception from a psychological reaction pattern involving withdrawal, fear, flight, and anxiety, and to the induction of lethargy and sleep. The response to analgesics of patients with severe pain may therefore not be very closely related to pain-threshold-raising mechanisms. It should be emphasised that in our work the word "threshold" applies to the dose of drug given and not the strength of stimulus.

The most satisfactory procedure would be to compare the potency of analgesics in patients actually suffering from pain, since in any case this is the final field of application. Intelligent coöperative persons with chronic pain can sometimes, in our experience (which confirms that of Keele 1948), give reliable interpretations of their sensation of pain, and can give assessments of the severity of pain which correlate well with variations in dosage of a given drug and with changes from one drug to another. But it is not always easy to find subjects with all the necessary qualifications, since chronic pain may arise from diseases which make accurate observations difficult, and the emotional reactions to continuous pain may render coöperation impossible. It was for these reasons that our work was directed to experimentally induced pain in man, and our method of testing may be regarded as intermediate between pain-threshold and clinical studies.

The purely subjective assessment of pain calls for comment. Some patients could describe 4 or 5 grades of intensity of pain quite readily and with apparent consistency. It was thought that what patients of various grades of intelligence and powers of description could do student volunteers and members of the academic staff might do as well, if not better. With experience and practice it was found possible to distinguish about 10 grades of ischæmic muscle pain, the greater fineness of discrimination being perhaps due to the fact that the pain was steadily increasing during a short time (10–15 min.), no feats of memory of previous intensities of pain being required. Moreover, the constant number of ischæmic muscular contractions ensured fairly comparable curves of pain intensity in different experiments.

Hardy et al. (1947) have made observations on a pain-intensity scale, using thermal radiation pain in the skin. They recorded 21 just perceptible steps between threshold sensation and ceiling pain. They have adopted as the unit of pain intensity the dol: 1 dol = 2 just-perceptible steps in discrimination of stimulus intensity. The whole range of pain intensity would thus equal $10^1/_2$ dols. Our distinction of only 10 grades of intensity of pain (instead of 21 grades) may be related to the differences in character of a deep as opposed to a superficial pain.

The importance of adequate control studies has been fully appreciated in the course of this work, and the injection of distilled water or subthreshold doses of the analgesics gave consistently negative results. It is true that an increase in sensitivity to morphine, pethidine, and physeptone was recorded, but this change only took place over a long time and (apart from the remarkable response of subject C. A. K. to morphine) was similar for these three drugs. When tests were made at short intervals there were no discrepancies.

It might still be suggested that, instead of subjective criteria, however well controlled, objective measurements of accompaniments of pain should be used. The rise of blood-pressure and increase of heart-rate described by Alam and Smirk (1937, 1938) and the diminution in electrical skin resistance (Thompson and Gellhorn 1945), all noted during ischæmic muscular pain, were considered but, after preliminary tests, were found to be of little value. First, the extent of such changes varies widely from person to person; secondly, such changes are very small or non-existent with mild or moderate pain; and thirdly, analgesics might affect these readings by mechanisms distinct from the central relief of pain.

This work has shown that individual variations in sensitivity to both relief of pain and development of side-effects may be considerable. It seems likely that these variations are important in relation to the therapeutic effectiveness of these drugs in the relief of pain in disease.

(1) Variations in sensitivity to analgesic action will mean that with a given dose some persons will get better relief of pain than others.

(2) Side-effects may arise much more readily in some people than in others. Indeed, in some persons side-effects may arise before analgesia is produced. Since, as shown here, the relations between analgesic action and side-effects vary in one person from one drug to another, it is easy to understand why one drug may be therapeutically more satisfactory than another. It is therefore difficult to generalise, and at present it is impossible to explain or to correlate the varied responses seen in different persons.

In patients the relief of pain is more complicated than in these experiments. Our subjects were volunteers interested in the work; it was always known that the duration of pain would be relatively brief—i.e., 15 min. or less—and, more important, that if the subject decided that the pain was intolerable he could instantly procure relief by releasing the cuff. In patients pain is naturally resented, its duration may be considerable, and its appreciation may be linked with anxiety about the disease causing the pain. In these circumstances relief of pain is probably due more to the psychological than to the threshold-raising component of analgesic drug action.

Digitized by Google

SUMMARY

A method of testing analgesics in man has been studied in four normal persons. Maintained ischæmic muscular pain has been produced in the forearm and assessed subjectively in grades of intensity of 1–10 units (1 = very slight, 10 = intolerable pain).

The drugs tested were injected intravenously when moderate pain (4–5 units) was present. Effective doses produced rapid transient relief.

The best method of comparing the potency of different analgesics was to find the smallest dose of each drug which reduced pain of 4–5 units' intensity. The comparative effects of morphine, pethidine, physeptone, and C.B.11 are reported. Changes in threshold doses with time are discussed.

The actions of nitrous oxide and cyclopropane on ischæmic muscular pain are described.

The analgesic effects of intravenous procaine have been shown to be mainly of central origin.

Thiopentone, benadryl, neoantergan, antistin, and tetraethylammonium bromide have definite analgesic actions but are on the whole much weaker than the recognised analgesics.

Individual variations with regard to analgesic action and the development of side-effects are discussed.

We wish to thank Mr. R. M. L. Dry and Mr. J. W. Markham for their most willing coöperation and patience in this investigation; Dr. F. Prescott and Dr. R. H. Thorp, of the Wellcome Foundation Ltd., for their help in providing supplies of physeptone, Hoechst 10582, and isoamidone; Glaxo Laboratories Ltd. for supplies of C.B.11; Dr. H. O. Schild for a sample of pure benadryl; and Dr. A. S. V. Burgen for helpful criticisms.

REFERENCES

Alam, M., Smirk, F. H. (1937) *J. Physiol.* **89**, 372.
— — (1938) *Ibid*, **92**, 167.
Allen, F. M. (1945) *Amer. J. Surg.* **70**, 283.
Conley, J. E., Schumm, H. C., Rosenbaum, F. F., Gaenslen, F. G. (1947) *J. Lab. clin. Med.* **32**, 1422.
Goetzl, F. R., Burrill, D. Y., Ivy, A. C. (1943) *Quart. Bull. Nthwest. Univ.* **17**, 280.
Gordon, R. A. (1943) *Canad. med. Ass. J.* **49**, 478.
Hardy, J. D., Wolff, H. G., Goodell, H. (1940) *J. clin. Invest.* **19**, 649.
— — — (1947) *Ibid*, **26**, 1152.
Harrison, I. B., Bigelow, N. H. (1943) *Ass. Res. nerv. ment. Dis.* **23**, 154.
Hewer, A. J. H., Keele, C. A. (1947) *Lancet*, ii, 281.
Keele, K. D. (1948) *Ibid*, July 3, p. 6.
Lundy, J. S. (1942) Clinical Anæsthesia. London; p. 392.
Macht, D. I., Herman, N. B., Levy, C. S. (1916) *J. Pharmacol.* **8**, 1.
McLachlin, J. A. (1945) *Canad. med. Ass. J.* **52**, 383.
Seevers, M. H., Bennett, J. H., Pohle, H. W., Reinardy, E. W. (1937) *J. Pharmacol.* **59**, 291.
— Pfeiffer, C. C. (1936) *Ibid*, **56**, 166.
Thompson, M. B., Gellhorn, E. (1945) *Proc. Soc. exp. Biol., N.Y.* **58**, 146.
Thorp, R. H., Walton, E., Ofner, P. (1947) *Nature, Lond.* **159**, 679.

NEBULISED PENICILLIN AND POST-OPERATIVE PULMONARY COMPLICATIONS

E. J. HOLBOROW M.A., M.B. Camb.
E. A. SPRIGGS B.M. Oxfd, M.R.C.P.
From the Postgraduate Medical School of London

IN thoracic operations for suppuration of the lung the use of penicillin inhalations to reduce the incidence of postoperative pulmonary collapse proved disappointing.[1] We report here the results of a similar use of penicillin in the rather different circumstances of abdominal surgery.

The patients were adults undergoing abdominal operations, including herniorrhaphy. Each was examined at least a day before operation and assessed as a "chest risk"—good, moderate, or bad. In each of these three categories alternate patients were treated with nebulised penicillin, the remainder serving as controls.

In the treated group at least three inhalations of penicillin (100,000 units each) were given in the 24 hours before operation. Further doses were given the evening after operation and the next morning. Since it was found that penicillin-sensitive organisms usually took 48 hours or more, after inhalations were stopped, to return to the respiratory tract, and since in most cases pulmonary collapse has its origin in the first 24 hours after operation,[2] this dosage of penicillin was thought sufficient as a minimum. Most of the patients, however, for reasons sometimes unconnected with the main experiment, received longer courses, either starting earlier or finishing later, or both.

Bacteriological examinations were made on swabs from the nose and throat, and on sputum when it could be obtained. Effective administration of penicillin, as reflected in the respiratory flora, was proved for each case in the treated group.

Patients were examined daily, after operation, by the same observer (E. A. S.) in all the cases. Clinical evidence of pulmonary collapse or consolidation, confirmed by radiology, was the criterion of complication. Pulmonary embolism, uncommon in the first week after operation, was outside the scope of the inquiry.

RESULTS

Bacteriology

In the penicillin-treated group the bacteriological changes followed a standard pattern. The first swabs taken after the start of inhalations gave a smaller total growth than the initial swabs. On the day of operation the upper respiratory tract was often superficially almost sterile, and any penicillin-sensitive pathogens which had originally been demonstrated—e.g., β-hæmolytic streptococci, *Strep. pneumoniæ*, *Staph. aureus*—could no longer be grown.

After two days' inhalations the multiplication of penicillin-resistant bacteria was usually advanced. These were predominantly organisms of the coli-aerogenes group, usually in pure culture, but sometimes associated with *Hæmophilus influenzæ* or other resistant bacteria. Return of penicillin-sensitive organisms while the inhalations continued was not observed. Multiplication of neisseria strains sometimes either preceded or accompanied the appearance of coliforms, but these strains were relatively insensitive to penicillin, requiring a concentration of 4–6 units per ml. for inhibition in vitro.

Similar changes were observed in those cases of the treated group which had pulmonary complications.

Complications

The incidence of pulmonary complications was as follows:

	Treated	*Controls*	*Totals*
Complications	10	6	16
No complications	34	38	72
Total	44	44	88

It will be seen that chest complications occurred *more* frequently in the treated group than in the controls, but the difference is not statistically significant.

If the administration of nebulised penicillin, among a much larger series of cases, were to reduce the number of chest complications to half, the expected incidence of complications in 88 cases would be as follows:

	Treated	*Controls*	*Total*
Complications	5·3	10·6	16
No complications	38·6	33·3	72
Total	44·0	44·0	88

A deviation as large as that of the observed incidence from the expected incidence would occur by chance only once in 150 times ($\chi^2 = 7{\cdot}40$; $n = 1$). It is therefore understood that nebulised penicillin, as administered in this series, would not substantially reduce the incidence of chest complications.

1. Findlay, C. W. jun., Sweet, R. H. *J. thorac. Surg.* 1947, **16**, 81.
2. Stringer, P. *Lancet*, 1947, i, 289.

Digitized by Google

The complicated cases in the treated group had a rather longer average duration of fever than those in the control group.

CONCLUSION

Our failure to reduce the incidence of chest complications may be explained in one of two ways. First, bacterial infection may have nothing to do with the production of the sticky phlegm which often blocks the air-tubes after operation. Or, secondly, and perhaps more likely, the influence of infection may be important, but a penicillin-resistant flora may be no more desirable—indeed may be more dangerous—than the natural one.

We wish to thank Prof. Ian Aird, Mr. M. R. Ewing, and Prof. Lord Stamp for supervising this inquiry, and Mr. J. W. Boag for his help with the statistics. Oxycillin atomisers were lent by Messrs. Oxygenaire Ltd.

TUBERCULOUS MASTOIDITIS TREATED WITH STREPTOMYCIN

REPORT OF A CASE

O. D. FISHER
M.B. Lond., D.C.H.
PÆDIATRIC REGISTRAR

E. A. MALKIN
M.R.C.S., B.Sc. Lond., D.L.O.
LATE HOUSE-SURGEON, EAR, NOSE, AND THROAT DEPARTMENT

KING'S COLLEGE HOSPITAL, LONDON

TUBERCULOUS infection of the middle-ear cleft is a grave condition, especially in infants; it is often complicated by facial palsy and may be followed by destruction of the labyrinth and by meningitis. The following case was treated by surgery and subsequently with streptomycin.

On Dec. 19, 1947, a female infant, aged 8 weeks, was first seen with seven days' history of right otorrhœa and two days' partial right facial paralysis. There was a profuse mucoid foul-smelling discharge from the right ear; the drum-head was not clearly seen, but there appeared to be a granulation which bled freely when touched with a probe. There was slight postauricular œdema. A well-developed right facial palsy was present, incomplete in the distribution of the upper division of the nerve. A submandibular gland on the right side was enlarged, but no preauricular or postauricular glands were palpable. There were no other abnormal physical signs, except that the spleen was just palpable.

On Dec. 21 the clinical appearance strongly suggested a tuberculous infection, and a cortical mastoidectomy was performed under basal paraldehyde and local infiltration with procaine. The skin and periosteum were œdematous; when the cortex was opened a large cavity full of foul-smelling necrotic material was found. After curetting, the lateral sinus plate, horizontal semicircular canal, and incus were clearly seen. The wound was closed, and a small inferior rubber drain was left in situ for thirty-six hours. Penicillin was given systemically, 25,000 units eight-hourly, until Dec. 28.

Streptomycin therapy was begun on Feb. 6, 1948, and continued for thirteen weeks. The dosage was calculated on the basis of 0·02 g. per lb. body-weight daily and given twelve-hourly by intramuscular injection together with 0·1 ml. of 2·5% procaine (Feldman et al. 1947, Cathie 1948, Medical Research Council 1948). The total dosage was 26·5 g. There was no evidence of toxic symptoms referable to the streptomycin at any time.

During the postoperative period the local treatment consisted of mopping out the meatus, but during February and March the meatus was syringed twice daily with hypertonic saline and eusol. The postauricular incision broke down, and a discharge persisted until the middle of March, when it healed for about three weeks. It then discharged again until the end of April, since when the wound has been soundly healed, but the scar is depressed.

The meatal discharge remained offensive and profuse until the third week in March, when it became gradually less, and it dried up completely a month later.

An improvement in the facial paralysis was first noted about the middle of January, and by the second week in March recovery was complete.

Histology.—Prof. H. A. Magnus reported on Dec. 22, 1947, that sections of material from the antrum showed granulation tissue and some areas of caseous necrosis, but no tubercle follicles, and that sections stained by the Ziehl-Neelsen method showed several groups of undoubted tubercle bacilli, the histological appearances of this material being those of a purely exudative lesion.

Bacteriology.—Culture of acid-fast bacilli found in the specimen of pus from the antrim on Dec. 22, 1947, yielded a human strain of *Myco. tuberculosis.*

Tuberculin Skin tests.—Tuberculin-jelly test negative on Dec. 29, 1947; Mantoux test 1/100,000 negative on Jan. 5, 1948, and 1/10,000 negative on Jan. 8; tuberculin-jelly test positive on Jan. 10.

Blood.—On Jan. 2 a blood-count showed 2,960,000 red cells per c.mm., Hb 58%. The erythrocyte-sedimentation rate (E.S.R.) was 27 mm. in the first hour (Payne). Two transfusions of 50 ml. of group-O Rh-negative blood were given via the internal jugular vein at this time.

Blood-streptomycin Levels.—On Feb. 10, the blood level eight hours after injection was 4 units per ml.; ten hours after injection, 2 units per ml.; and twelve hours after injection, less than 0·25 unit per ml.

Cerebrospinal Fluid (C.S.F.).—Cells 4 per c.mm., protein 30 mg. and chlorides 760 mg. per 100 ml., culture sterile.

Radiograms of chest on Dec. 19, 1947, and May 18, 1948, were clear.

Urine.—No abnormality was found at any time.

Subsequent weekly blood, urine, and C.S.F. examinations were made until the patient's discharge from hospital, when the E.S.R. was 14 mm. in the first hour, Hb 62%. The C.S.F. findings remained constant throughout.

From the past history no source of infection could be ascertained; the child had been born in hospital and subsequently nursed at home. No mouth-to-mouth artificial respiration had been used, and initial feeding was by the breast, later supplemented with a half-cream dried milk. All chest radiograms of immediate contacts were clear.

DISCUSSION

The case is interesting in that streptomycin was used after a cortical mastoidectomy, with apparent resolution in fourteen weeks. Souper (1933) recorded 36 cases of tuberculous mastoiditis in which 17 of the patients were aged under 6 months, and 29 under 12 months, with a mortality of 59% among the first 24 cases treated by radical mastoidectomy. The remainder, treated by a Wilde's incision, a cortical mastoidectomy, or a radical mastoidectomy without a plastic meatal procedure, had a mortality of 36%. This latter and more conservative approach was also advocated by Ormerod (1939), who pointed out that, in acute cases of mastoiditis diagnosed preoperatively as tuberculous, it is usually wise to perform a cortical mastoidectomy and to await healing, which generally takes place after several weeks' dressing. It is also advised that the postauricular wound should be left open and packed with gauze through the meatus and the wound. The radical operation can then be performed if the discharge persists. There also seems to be a place for Wilde's incision in severely ill children with a subperiosteal abscess, to precede the opening of the mastoid.

It remains to be seen whether streptomycin therapy will altogether obviate the need for radical exenteration in these cases and will reduce the high mortality of this condition.

Our thanks are due to Dr. Wilfrid Sheldon and Mr. W. I. Daggett for permission to publish this case, and to Dr. I. A. B. Cathie for the supply of streptomycin, advice regarding dosage, and estimations of blood-streptomycin levels.

REFERENCES

Cathie, I. A. B. (1948) *Post-grad. med. J.* **24**, 351.
Feldman, W. H., Hinshaw, H. C., Karlson, A. G. (1947) *Amer. Rev. Tuberc.* **55**, 435.
Medical Research Council (1948) *Lancet*, 1948, i, 582.
Ormerod, F. C. (1939) Tuberculosis of the Upper Respiratory Tracts. London.
Souper, H. R. (1933) *Proc. R. Soc. Med.* **26**, 1585.

Digitized by Google

Preliminary Communication

TRIGEMINAL NEURALGIA TREATED WITH CUPRELONE

IN the late war the Germans produced a copper compound of low toxicity to serve as a substitute for gold salts. This substance, cuproallyl-thiourea-sodium benzoate, which contains 19% copper, is now manufactured in this country under the name of 'Cuprelone' and is obtainable in dry ampoules containing 10 to 100 mg. The powder is dissolved in sterile distilled water for intravenous injection. The salt is secreted in the liver and most tissues show an increased copper content after its administration. Excretion is slow and may last two months.

van Ravesteyn[1] gave the salt intravenously in 100 mg. doses (19 mg. of copper) and produced a rise in the blood-copper level for two hours after the injection. Probably all the extra copper is excreted in the next two or three weeks.

The observations made by workers that copper was useful in preventing swayback, a demyelinating disease of sheep, led Campbell et al.[2] to try copper sulphate in the treatment of disseminated sclerosis, without success. Copper sulphate had the disadvantage of being a gastric irritant and in some cases it caused vomiting and had to be discontinued. The introduction of cuprelone offered an organic copper salt which was free from this disadvantage; so it has been tried in disseminated sclerosis. Although there has been little evidence of improvement in this disease, it was noted in a patient with disseminated sclerosis who also had severe trigeminal pain, that the pain was alleviated immediately after an injection of cuprelone.

On the basis of this observation cuprelone has been tried in a few cases of classical trigeminal neuralgia, and in some of them there appeared to be a decrease in the number of attacks and a lessening of pain. Trigeminal neuralgia normally waxes and wanes and may often improve on admission to hospital with rest in bed; but, even when allowances have been made for this, it is considered that some cases responded satisfactorily to intravenous cuprelone. The cases have been assessed by charting the number of attacks of pain against the time in days (figs. 1–4). This shows a response both to a series of injections and to single injections. The results, though varied, are thought worthy of publication.

1. van Ravesteyn, A. H. *Acta med. scand.* 1944, 118, 163.
2. Campbell, A. M. G., Daniel, P., Porter, R. J., Russell, W. R., Smith, H. V., Innes, J. R. M. *Brain*, 1947, 70, 50.

CASE-RECORDS

Case 1.—A male casemaker, aged 43, first attended the Bristol Royal Infirmary in January, 1947, with severe shooting pain in the left side of the face and lower gums. He had first noted severe pain when washing his face, and this had persisted ever since, with anything up to 30 attacks a day, precipitated by eating, washing, or speaking. The patient appeared to have a typical trigeminal neuralgia, and he was obviously frightened of speaking and moving the lower jaw. Ten years earlier he had suddenly lost the vision in his right eye; this had lasted 6 weeks and then completely recovered. For $3^1/_2$ years he had noted increasing stiffness in both legs and had been treated by his doctor for rheumatism. It was only when the severe pain in the face began that he was forced to attend hospital.

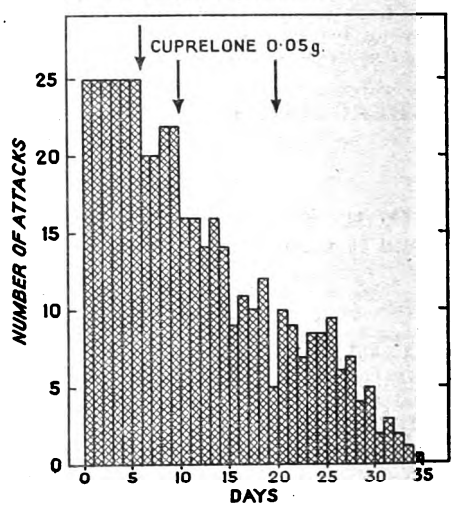


Fig. 2—Trigeminal pain treated with a total dosage of 0·15 g. of cuprelone in 35 days (case 2).

He had nystagmus on looking to the right, and there was spasticity of both legs, with increased reflexes, plantar reflexes being equivocal on the left and extensor on the right. Disseminated sclerosis was diagnosed, and the trigeminal pain was considered to be due to a plaque involving the fifth-nerve nucleus.

Fig. 1 shows that the patient reacted satisfactorily to 'Trilene' and later to cuprelone injections. Towards the end of the treatment he had paræsthesiæ in the legs, probably a result of the copper injections. Apart from this his urine, blood-count, and cerebrospinal fluid remained normal throughout treatment. Follow-up shows that he has had no return of pain in the year and a half since treatment.

Case 2.—A baker, aged 79, had had severe pain in the right side of the face for 30 years, with periods of freedom, but becoming more severe lately. In April, 1947, he was

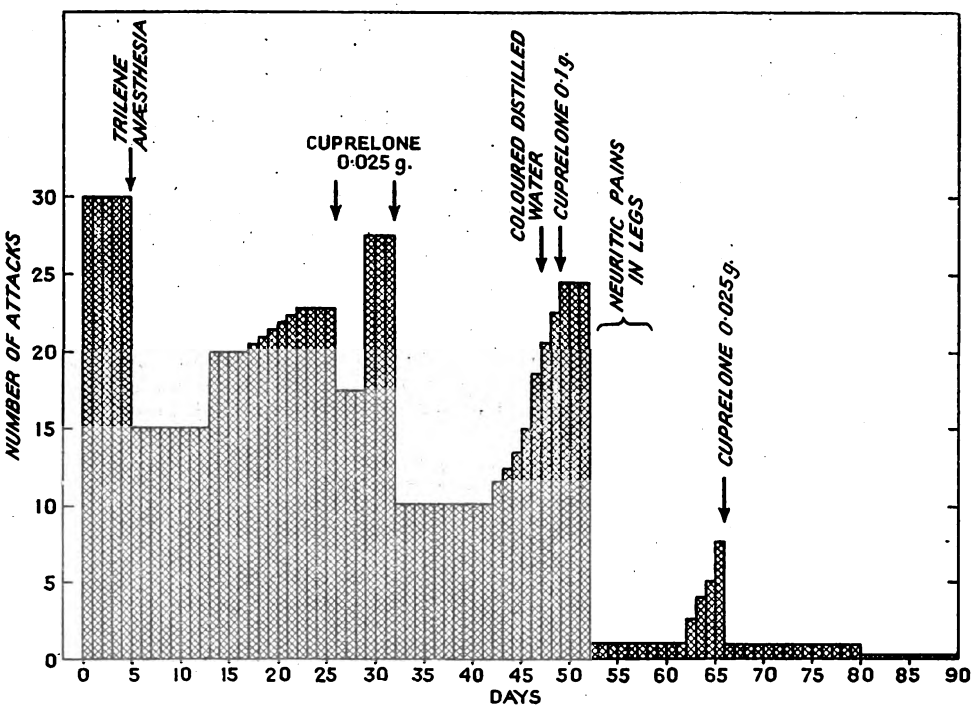


Fig. 1—Trigeminal pain created with a total dosage of 0·175 g. of cuprelone in 90 days (case 1).

Digitized by Google

getting attacks about every hour, precipitated by speaking or eating. He had one brother who had also had trigeminal neuralgia.

He showed no abnormal physical signs apart from the fact that he was obviously having periodic severe pain, for which he got relief by rubbing his face to the extent of producing conjunctivitis on this side. He was generally fit.

Under a course of injections of cuprelone the patient rapidly improved (fig. 2); he was discharged having lost his pain and now twelve months later he has remained more or less free from pain.

Case 3.—A housewife, aged 66, had had severe intermittent pain of the right side of the face for 12 years, brought on by eating, washing, removing the denture, or talking. Occasionally the attacks appeared to arise spontaneously. The present attack began 6 weeks before, and had continued up to admission to hospital in July, 1947. Through the whole course of her illness the patient had never had a remission of pain for more than 3 months.

There were no abnormal physical signs, except a slight loss of weight owing to the difficulty in eating. There was a definite trigger point for production of pain on the upper lip at the junction of the lip with the nostril.

The patient improved with a course of cuprelone injections (fig. 3), and was discharged free from pain. A year later she wrote that she had never felt better.

Case 4.—A housewife, aged 71, had had severe pain in the left side of the face 4 months before admission to hospital in June, 1947, followed by severe attacks of burning pain in the right side of the face, typical of trigeminal neuralgia and brought on by rubbing, touching, and eating. In her previous history, the only important factor was that she had had gout.

No abnormal physical signs were noted, and the patient was not so severe a case as the three previous ones. Her general condition was good.

After a course of cuprelone injections (fig. 4) she was discharged free from pain; 3 months later her doctor wrote that she had had a relapse, which had responded to a sedative mixture.

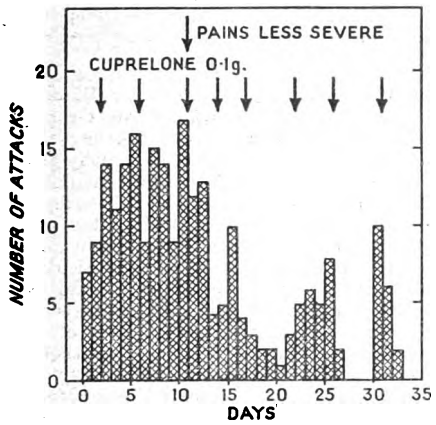


Fig. 3—Trigeminal pain treated with a total dosage of 0·8 g. of cuprelone in 33 days (case 3).

DISCUSSION

In these four cases the injection of cuprelone was followed by relief of pain: in some cases single injections of 50 or 100 mg. seemed satisfactory; in others more distinct relief followed a course of injections of 800 mg. in 6 weeks. All the patients were satisfied that the injections had materially lessened the number of their attacks and the severity of their pain. In a case of malignant bone disease cuprelone did not relieve the pain.

In case 1 an injection of distilled water had no effect on the pain, though the patient was unaware that there had been any change in the injection. In this case cuprelone relieved the pain as satisfactorily as did trilene. The dosage has been varied experimentally, and a higher dosage may possibly be given without ill effect. Case 1 showed severe paræsthesiæ in the legs in the middle of the course, and this may have been caused by copper. There has been no evidence of leucopenia or of renal damage. Of these four patients three remain well 6 months later, but one has relapsed.

Cuprelone has been tried in nine other cases. In one it appeared to have no effect, and in two the effect was doubtful, but in six the result appears to have been satisfactory, and it is felt that the action of cuprelone is worth further study. It may have specific effects on the trigeminal-nerve nucleus, as triethylene and stilbamidine appear to have. If this is true, a modification of the drug in structure and dosage may play a useful part in the relief of a painful malady.

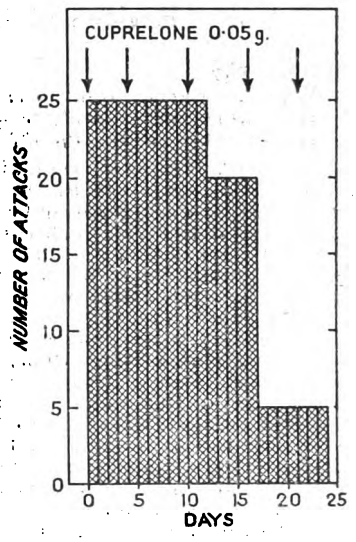


Fig. 4—Trigeminal pain treated with a total dosage of 0·25 g. of cuprelone in 30 days (case 4).

SUMMARY

Intravenous injections of cuprelone have been given in thirteen cases of trigeminal pain, and in some of them the pain was relieved.

Toxic effects were negligible.

Owing to psychological factors, the results must be interpreted cautiously.

Cuprelone may possibly act directly on the trigeminal nucleus.

My thanks are due to Bayer Products Ltd. for supplies of this drug.

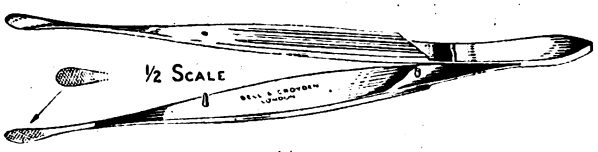
A. M. G. CAMPBELL
D.M. Oxfd, M.R.C.P.

Bristol Royal Infirmary.

New Inventions

DISSECTING FORCEPS WITH SPATULATE ENDS

THIS dissecting non-toothed forceps is a modification of McIndoe's forceps and is adapted from the patterns commonly in use in the United States. It is useful for



holding intestines during anastomosis and also in suturing the various layers of the abdominal wall. As the cross-serrated spatula-like ends do not injure the tissues when used during dissection or suturing, it has many advantages over the ordinary forceps employed today.

The forceps has been carefully made to my instructions by John Bell & Croyden, London.

RODNEY MAINGOT
F.R.C.S.
Surgeon to the Royal Free Hospital and the Southend General Hospital.

"... The great French clinicians of the nineteenth century taught, as a matter of course, that there were two stages in the development of alcoholic cirrhosis. The first, in which the liver was enlarged and infiltrated with fat, they called steatosis of the liver: the second, in which the organ was small and fibrotic, they termed portal, atrophic, or Laennec's cirrhosis. For some reason this knowledge did not take root and withered under the sterilising error which conceived hepatic fibrosis as a single entity—cirrhosis of the liver—instead of the similar end result of different initial injuries."
—Prof. H. P. HIMSWORTH, *Science Progress*, 1948, **36**, 577.

Digitized by Google

Reviews of Books

Cardiography

WILLIAM EVANS, M.D., D.SC., F.R.C.P., physician to the cardiac department, London Hospital. London: Butterworth. 1948. Pp. 132. 25*s*.

Dr. Evans's book is in two parts, the first dealing with the common abnormalities of the electrocardiogram and the second with records of heart sounds. The electrocardiograms illustrating the first section are accompanied by a minimum of text and little or no theory as to the mode of production of cardiographic changes, but the student who applies himself to the tracings and description will gain a first-class introduction to the subject. The second section, on phonocardiography, is very largely the original work of the author, who has done much to clarify and advance this aspect of cardiology. The special value of this method is in the diagnosis of some valve lesions, and, according to Evans, in its ability to distinguish the innocent from the significant murmur, and to classify added heart sounds. The subject is still in an early stage of development, but this account is the clearest and most rational we have seen. The conclusions drawn are based on very extensive observations, and whether or not they are confirmed by further investigations they will certainly prove a valuable stimulus to further work.

The records illustrating both sections of the book are nearly all of flawless quality.

Recent Advances in Surgery

(3rd ed.) HAROLD C. EDWARDS, C.B.E., M.S., F.R.C.S., surgeon and lecturer in surgery, Kings College Hospital London. London: J. & A. Churchill. 1948. Pp. 437. 24*s*.

NEARLY twenty years have passed since the second edition of this book was published, and Mr. Edwards must have found it hard to select the subjects for his new one. His choice will be generally acceptable. Possibly a more satisfying treatment would have been to cut down the number of subjects and go into them a little more deeply, but the student preparing for an examination will no doubt prefer the arrangement as it is. The alimentary tract claims the largest section of the book and is well covered. In addition to this section, and a preliminary chapter on general subjects including the healing of wounds and fluid balance, Mr. Edwards himself has been responsible for a section on diseases of blood-vessels and a miscellaneous one dealing among other things with the thymus and the prostate. Three other authorities contribute chapters on the more specialised branches of surgery: Mr. R. C. Brock on the thorax (confining himself to the surgery of the heart and bronchial carcinoma); Mr. D. W. C. Northfield on neurosurgery; and Sir Stanford Cade on the radiotherapy of malignant disease. Altogether this is a most useful book, not only for the student but also for the busy practising surgeon who must keep up to date.

Practical Bacteriology, Hematology, and Parasitology

E. R. STITT, M.D., PH.M., SC.D., LL.D., surgeon-general, U.S. Navy, retd; PAUL W. CLOUGH, M.D., physician-in-charge, diagnostic clinic, Johns Hopkins Hospital; SARAH E. BRANHAM, M.D., PH.D., SC.D., senior bacteriologist, National Institute of Health; and contributors. London: H. K. Lewis. 1948. Pp. 991. 50*s*.

IT is ten years since the previous edition of this well-known practical textbook appeared and it is not surprising that in some respects this tenth edition is almost a new book. Still of reasonable size and price, it remains a remarkable compendium of facts and figures that the clinical pathologist and physician need to know but cannot always carry in their heads. The new bacteriology section contains many good tabular summaries. The nomenclature adopted is that of the 6th edition of Bergey's Manual, except in the case of the salmonellas. Up-to-date techniques, like the yolk-sac material method for distinguishing the different rickettsiæ, are fully represented; and it may be noted that infective hepatitis and homologous serum jaundice are placed among the filtrable virus diseases. The section on medical mycology is a well-illustrated account of a group of conditions some of which are rare in this country. Hæmatological methods are well described, and the authors are decided about which they think best: the modified Neubauer ruling is preferred for hæmocytometry, and either a photo-electric colorimeter or a Sahli instrument for hæmoglobinometry. Most American textbooks have given up Haldane's method now. The illustrations, except for the plate showing the blood picture of monocytic leukæmia, are not very good, and the explanation of the hæmorrhagic diseases is seriously out of date.

The tropical and parasitology sections, and those that deal with insects, poisonous snakes, and fish, are as good as before, and there are some first-class plates of malarial parasites. A new section on vitamins is provided; and a useful table sets out the variation of some important constituents of the blood—such as urea, sodium, and calcium—in various diseases. This is a welcome revision well able to take the place of its predecessor.

Post-Mortem Appearances (5th ed. London: Oxford University Press. 1948. Pp. 308. 8*s*. 6*d*.).—This practical little pocket-book has been extensively and well revised to maintain its usefulness as a guide to students and those having to perform autopsies without advice and assistance. Dr. Joan Ross is as concise, lucid, sound, and practical as ever, and her book contains a remarkable amount of information couched in good terse English.

An Apple a Day (London: Cassell. 1948. Pp. 195. 10*s*. 6*d*.).—Those who have read *Go to the Country* and have discovered Dr. Philip Gosse's humour and joy in natural sights and sounds will be prepared for this successor. He narrates his professional success and non-success with equal gusto. (His habit of taking a long holiday after an unequal contest with his professional examiners must be noted, but whether this was of a consolatory character, or, in his mind, a reward for work well done, he does not specify.) The book as a whole is an odyssey of adventure, taking us all over the world; but it is also full of wise sayings and bears the stamp of a keenly observant outlook. Dr. Gosse notes and comments tellingly on many apparent trivialities in life which most of us take for granted. There is a certain carefree irresponsibility about him which gives his book an atmosphere and charm of its own.

The Way to Natural Childbirth (Edinburgh: E. & S. Livingstone. 1948. Pp. 124. 7*s*. 6*d*.).—Since Dr. Grantly Dick Read published *Natural Childbirth* over fifteen years ago a new school of obstetrics has arisen. It is healthy that the technique of an unorthodox clinical method should be elaborated by enthusiastic disciples, and Mrs. Helen Heardman is evidently one of them. She practises and writes as a physiotherapist who has become interested in obstetrics, and this approach carries a risk of emphasis on a meticulous régime of physical preparation. In their written form, her instructions have an austerity which would disturb the sensitive minds of many expectant mothers; while some of the illustrations would certainly upset all anatomists. Nevertheless the book should be useful to the teacher, and especially the physiotherapist of an obstetric unit; for, though it is largely a synopsis of the work of others, it also describes the author's own experience, both personal and professional.

Malaria Control by Coastal Swamp Drainage in West Africa (London: Ross Institute of Tropical Hygiene. 1948. Pp. 97.).—Before and during the early days of the war, Apapa in the urban area of Lagos was notoriously malarious. A vessel making a stay of only one night alongside Apapa wharf would, within a couple of weeks, have many of its crew down with fever, and 80% of all ranks of an anti-aircraft battery stationed there in 1942 contracted malaria within three months of their arrival. Extensive swamp-drainage schemes and mosquito control by engineering methods were instituted by the Services, and matters began to improve. Within a comparatively short time malaria had ceased to be an almost invariable sequel to a visit to the area, and in a year or two it became relatively rare. In this small volume Dr. A. B. Gilroy, now principal of the India branch of the Ross Institute, gives an account of the problems confronted and of the methods whereby this very considerable achievement was reached. It is well illustrated by lively diagrams, plan drawings, and fine photogravure plates, and will be valuable to all concerned with like problems.

Digitized by Google

Modern treatment of VARICOSE CONDITIONS

Modern Technique embraces Ligature, Injection and firm Compression Bandaging

Suitable Compression Bandages are:

ELASTOPLAST * SEMIPLAST * ELASTOCREPE
ELASTOLEX * DIACHYLON/ELASTOCREPE
VISCOPASTE * ICHTHOPASTE

All of which are made by T. J. SMITH & NEPHEW LTD.,
Neptune Street, Hull

a **single** *supplement*
for **multiple** *deficiencies*

COMPLEVITE

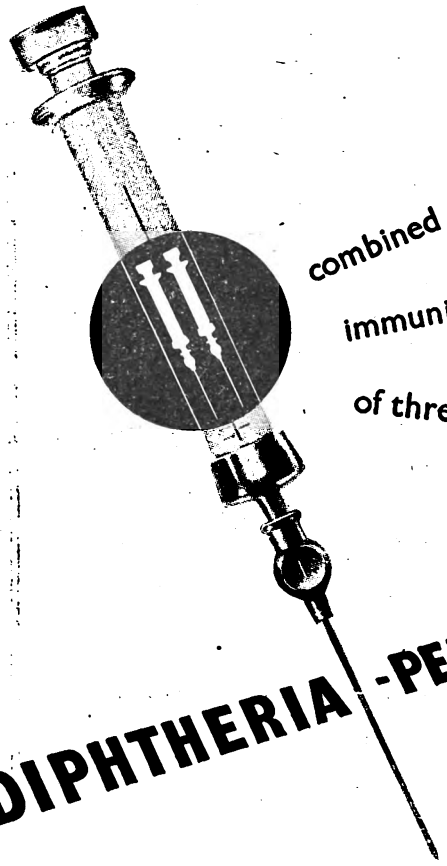
CLINICAL USES

As a general dietary supplement: in restricted diets, gastro-intestinal diseases: in fluid and light diets: in low fat and other special diets: hyperthyroidism and other states with raised B.M.R.: in chronic infections: throughout convalescence. Also for replacing other preparations of more limited application where full therapeutic doses of the vitamins are not required.

* Amounts contained in the recommended adult daily dose of one tablet of each colour three times a day.

Vitamins Limited
Upper Mall, London, W.6.

Digitized by Google



combined diphtheria-whooping cough

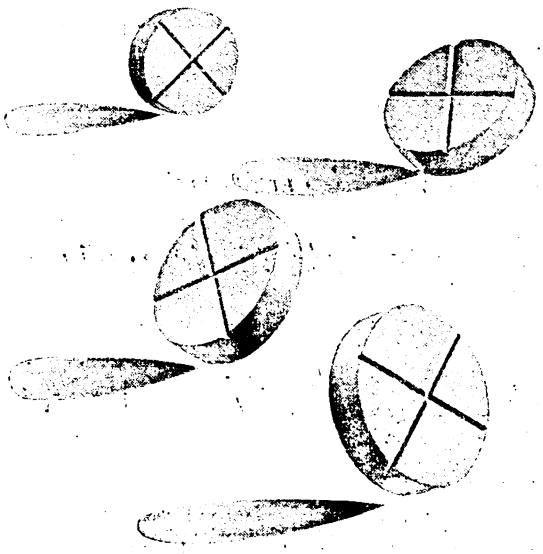
immunisation in a single course

of three injections

DIPHTHERIA-PERTUSSIS PROPHYLACTIC

GLAXO

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX. BYRon 3434



Three or four months may yet pass before the chilblain season is at its height. But *active* anticipation of the wintry weather can make the future a great deal brighter for those inveterate chilblain cases. Started now, a daily routine of four Ostocalcium Tablets will make an essential contribution towards the healthy capillary circulation so vital in withstanding the cold. Ostocalcium exerts a controlling influence on the permeability of the capillaries, preventing the exudation of fluid into the tissues that causes the characteristic swelling and inflammation. And the Ostocalcium formula takes full account of the need for vitamin D in calcium therapy, each tablet containing 500 i.u. of the vitamin with 125 milligrams of calcium.

course of action against chilblains ...

GLAXO OSTOCALCIUM TABLETS

In bottles of 50 and tins of 100

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX. BYRon 3434

Digitized by Google

THE LANCET

LONDON: SATURDAY, OCT. 30, 1948

Blood for Transfusion

THE National Blood Transfusion Service has lately been criticised in our correspondence columns on the ground of failure in its primary task, which is to supply blood in sufficient quantities, and of the right groups, to hospitals and other users. Like most other organisations at the present time, the service is of course capable of improvement; and there have been big difficulties to overcome in many areas. But there are already considerable achievements to its credit, and the collection of blood has much improved, especially in certain areas. For example, in the area covered by the two London blood-supply depots 36,522 donors were bled in the second quarter of this year, compared with 22,366 in the last quarter of 1946; and for the whole of England and Wales the figure rose from 65,532 to 98,055.

The panel of donors in England and Wales on June 30, 1948, showed an increase of about 110,000 over the figure for Dec. 31, 1946, and represented some 75% of the estimated optimum, assuming that donors are bled only twice a year. Certainly many more donors are needed; but it seems improbable that the methods used in France, as described by Dr. PINEY, would meet with much success in this country. The issue of chits to enable donors to buy extra rations amounts almost to payment; and, as Dr. POPHAM points out, this form of inducement might have to be replaced, when rationing ceases, by a cash equivalent, which would finally kill the voluntary spirit. Moreover, experience suggests that most of those who say that lack of good food prevents their giving blood—and this reason is rarely given—are in fact people who are already receiving extra rations by reason of their employment: the excuse is but seldom heard from the overworked and comparatively underfed housewife. The only tangible reward at present received by the donor is a neat booklet—rather like the pre-war driving licence—and a certificate for each donation. In addition he is in future to be issued with special badges after ten donations, after twenty-five, and after fifty. But it is questionable whether these badges will be much displayed, for most donors are self-effacing and unemotional about their contribution; and the appeal to sentiment, used with considerable success during the war, is now best replaced by a straightforward account of what blood-transfusion can do, and to what extent the hospitals rely on the help of local donors. To this end the National Blood Transfusion Service has lately begun to issue to all donors, when they give blood, a small illustrated brochure setting out the facts and appealing for increased support. The aim has always been to make the giving of blood an informal occasion; sessions, whether held in hospital wards, village halls, or factory canteens, have the atmosphere of a tea-party. More can and should be done on these lines. Surely it is high time that A.R.P. stretchers, wooden trestles, and drab Army blankets were replaced by equipment more pleasing to the eye and more fitting to a permanent peace-time service. The time has come, too, for the nurses and drivers to be given a distinctive uniform.

Though the demand for blood would doubtless be greater if there were unlimited supplies, the National Blood Transfusion Service can claim at least to be meeting essential needs, since the number of bottles collected during the June quarter exceeded the number used by almost 21,000. Most of this excess was made into dried plasma, and a large proportion was "carried forward," for issue during the next quarter. Any shortages, therefore, are likely to be temporary and local, and particularly of group-O blood; for more than half the blood issued is of this group. To relieve this difficulty, hospitals might well improve their arrangements for blood-grouping, so that wherever possible homologous-group transfusions were given. It might be feasible to determine the ABO group and Rh type of every patient on admission, so that only a cross-match would be required when blood was given; and group-O Rh-negative blood, which is apt to be scarce, could be reserved for patients who must have it. The success that regional blood-transfusion officers have had in persuading hospitals to use homologous blood is evident from the fact that in the past twelve months the proportion of group-O blood has fallen from 60 to 53% of the total issued, while the proportion of Rh-negative blood has risen from 4·5 to 9·2% of the total. One of the aims of the service since mid-1946 has been to encourage, and (where necessary and possible) to perform, Rh tests on women before childbirth; and since the last quarter of 1946 the number of tests made quarterly by the service has risen from some 26,000 to over 56,000—an increase of about 112%. Another aim has been to encourage the use of concentrated or packed red cells for the treatment of anæmias, and between the last quarter of 1946 and the second quarter of 1948 the blood employed for these preparations rose from 1469 to 3452 bottles—an increase of 135%.

In the United States and Canada relatively more blood is used for transfusion than in this country; and no doubt the demand here will grow. As this happens, it will be increasingly important for consultants and housemen to see that blood is used only when it is really needed. There is undoubtedly some wastage from indiscriminate transfusion, blood being given without sufficient indication that it may really benefit the patient. Even more wasteful is the practice of ordering an unreasonable number of bottles, to be cross-matched and set aside against the patient's later need; often these bottles are held in reserve until the expiry date and are never used. Both these causes of waste would be largely eliminated if replacement involved something more difficult than a telephone call to the nearest regional transfusion centre, and if all those who ordered transfusion remembered that they are handling a gift made at sacrifice of time and energy. Dr. POPHAM in our issue of Sept. 25 urged that more should be done to

Digitized by Google

enlist the help of patients' relatives, who are often willing to join a panel and replace the blood used. But he rightly said that this kind of effort cannot be made by one person, for it requires the interest and support of the whole hospital staff. Interest and support are in fact the outstanding needs of the whole blood-transfusion service, and criticism comes best from those who help it most.

Specificity of Infection

A GOOD understanding of the pathology of infection cannot be gained without studying the part played by the host. In a natural desire to exploit new methods of examining the physiology and biochemistry of bacteria and viruses this has sometimes been forgotten, and we therefore welcome the timely message of Professor WILSON SMITH'S presidential address last week to the Royal Society of Medicine's section of comparative medicine. He has rightly redirected attention to the unsolved puzzles of host and tissue specificity in infections. Why, for example, is the leprosy bacillus unable to grow except in man? Why is the Algerian sheep resistant to anthrax while other sheep are susceptible? Why do some people have several colds a year while others escape?

These questions have fascinated their students ever since EHRLICH'S brilliant observations, deductions, and guesses started the debate which still continues; and knowledge of them has now reached a stage when a reasonable amount of theorising offers the best chance of designing the crucial experiments required. In broad terms, as WILSON SMITH pointed out, specific associations of infecting agents with species, races, individuals, tissues, or cells depend on whether the host cells can participate in biochemical reactions with the infecting parasite or its products. "Extrinsic" factors may decide or influence the issue: for example, the right or wrong portal of entry; the presence or absence of an essential vector; whether the host's nutrition is good or bad, or his metabolism active or sluggish; whether the host has had previous contact with the infecting agent; and whether his body fluids stimulate or suppress the invader's growth. About some of these factors a fair amount is known, and others are being purposefully investigated. But "intrinsic" factors, intimately connected with cell structure and function, are more difficult to explore, and it is about these that speculation is most required.

To make a start with our guesses, we may profitably consider some of the recent discoveries about viruses. The association between a virus and a host cell it has parasitised is particularly close; indeed the virus cannot grow in nature or in artificial culture unless it is able to enter a living cell. It is of great interest, therefore, to learn that between some viruses and cells specificity of association does not depend on the whole cell or virus but on a particular component. Thus both living and heat-killed influenza virus can agglutinate the red blood-cells of the chick; but the next reaction, elution of the virus from the cell, is not accomplished with heat-killed virus, because this has lost the enzyme required to disintegrate the part of the red cell (the receptor) which holds on to the virus. If red-cell receptors for influenza virus are destroyed by treatment with *Vibrio cholerae* mucinase, the virus cannot be adsorbed to the cell and the cell cannot be infected.[1] It is a fair guess that the transient insusceptibility observed with some viruses may coincide with the stage when the cell, having rid itself of infecting virus and specific receptor in a single act (elution), cannot be reinfected until it has regrown its receptors. Among bacteriophages, which may be accepted as viruses for our argument, specificity is narrowed even to variants of a single strain of bacteria. A culture of bacterial host cells susceptible to lysis may be readily transformed to one in the insusceptible state, and the change may depend on loss of specific cell receptors or on their being masked by new components, as in the loss or gain of an antigen. Inactivated phage, by blocking specific receptors of the host cell, may prevent lysis by active phage whose attachment has been made impossible by the "interference" of the inactivated phage. This perhaps explains how modified viruses may act as specific immunising agents against virulent forms of their own strain, and may sometimes confer insusceptibility on others whose demonstrable relationship is remote. But simple blockage of cell receptors will not explain all we know of bacterial insusceptibility to phages, and LURIA and DELBRÜCK supposed that there may be competition among phages for a single key enzyme present in the host cell in such small amount that it may be deviated by even one particle of inactivated phage.

The lifelong resistance to reinfection conferred by some viruses probably depends on continuous carriage of the virus in the host cells and its transmission to daughter cells—a phenomenon well established for lysogenic strains of the bacillus group which transmit phage to cells arising even from their spores. If similar perfection of cell-virus symbiosis is possible in man, the many unexplained transient fevers of childhood may represent only the acquisition of an unidentified virus which, when it has settled in its appropriate place, may have an important part to play in developing general or specific resistance. We now know that viruses may enter and grow in a cell without causing much or any constitutional disturbance, especially if—as in recurrent herpes—the balance of events is not disturbed by some intercurrent infection or other upsetting event. In addition, viruses show great powers of adaptation if they are given enough opportunity to parasitise a new host or tissue. This was well shown in the gradual adaptation of human influenza to the mouse via the ferret. From the ferret adaptations were also made to the guineapig and rat, and, in these species the infections were symptomless. Similarly with rinderpest virus, strains were adapted from oxen to goats and rabbits, and the infectivity for oxen of a strain undergoing goat adaptation was found to depend on the number of goat passages it had undergone—remarkable evidence of the plasticity of the virus and of a quantitative aspect to the process of adaptation.

Putting all these guesses together, WILSON SMITH argued that infection, with all its enzyme interactions, requires physical linkage of virus to host cell, and that this is possible only if the molecular configurations of virus and cell allow close enough apposition. The explanation of complete specificity may well be that the virus has a surface shape so

1. Burnet, F. M. *Lancet*, 1948, i, 7.

Digitized by Google

peculiar that it can find only one type of cell into which it can fit. Such a conception, after all, is accepted for the interactions between antigen and antibody. Complete specificity of this kind may later be lost through adaptations to other cells of the same host or to other hosts. Moreover, just as a cell adapted to produce antibody globulin of a particular shape transmits this property to its descendants, so the later generations of an adapted virus can reproduce the new shapes first learned by their enterprising ancestor.

At the risk of over-simplification, we may say that many features of infection specificity probably depend on whether food is both available and accessible to the parasite. If an innkeeper wants to offer true hospitality to a fastidious guest of unusual proportions he will see to it that the guest's favourite meal is on the table, but he will not think his duty discharged until he has provided a chair of a size and shape that will allow his guest to reach the table in comfort. Nor, while his guest is eating, will he fill the room with stick-at-nothing ruffians who make no secret of their desire for a square meal of the kind on the table. If the establishment fails in such matters, the innkeeper need not expect his guest to stay, and still less to call again, recommend the place to his friends, or enjoin his children and grandchildren to confer their exclusive patronage on the hostelry in memory of the services afforded him.

Return to Philanthropy?

IT is presumably inevitable that with our advance towards social security, sponsored by the State, some of the light should seem to fade from voluntary effort. Now that we have attained to social insurance for all, and so much else, the giant evils of the past begin to look less formidable, and many of those engaged in voluntary effort may even feel a little sad. By contrast with the enthusiastic gatherings of the hospital contributory scheme of a decade ago, the meetings of a regional board may seem to lack the old zest. Yet, at least in the National Health Service, the volunteer has opportunities of usefulness as great as any in former days. And we know that loneliness and failure and misery will still demand help of many kinds, despite all the State can do.

Into this field Lord BEVERIDGE has moved in his latest report entitled *Voluntary Action*.[1] Having been reluctant to see the approved societies by-passed in the administrative machinery of social security, he has now collected a group of helpers and has produced a readable survey, not only of mutual insurance in all its forms, but also of the much wider subject of philanthropy today as it passes from the old world into the new. The first section of his inquiry is concerned with the motive of mutual aid, mainly as illustrated by the history of the friendly societies. He believes that there will still be a large scope for insurance above the minimum: it is likely that the societies will find a strong desire for higher benefits in sickness, above what the State gives, and especially during short periods of incapacity. A long section entitled "The philanthropic motive in action" traces the controversy between ARTHUR HOBHOUSE and JOHN STUART MILL on the reconciling of testators' wishes with the public interest. HOBHOUSE held that the public, in dealing with charitable trusts, must have the right to decide the particular use to which a testator's benefactions are to be put, and that there must always be "a living and reasonable" owner of property to manage it according to the wants of mankind. Taking HOBHOUSE's view as his criterion, Lord BEVERIDGE passes in review the work of the half-dozen great general trusts—the Nuffield Foundation, the Pilgrim Trust, and the others, and, in its slightly different category, King Edward's Hospital Fund for London. These trusts fulfil the necessary conditions, he says. They earn his approval; and indeed what other verdict could possibly have been given? But when he comes to deal with the older and numerically much larger group of miscellaneous charities he strikes a different note. The time has come, he thinks, when the mild and legalistic approach embodied in the powers of the Charity Commissions should be replaced by a much more radical plan. Might not many of the older charities be swept into the net and redesigned to meet current needs? Definite recommendations are made. The appropriate authority should have power, with the consent of the charity concerned: (1) at any time to make a scheme for its administration on the cy-près principle; (2) after fifty years to make a scheme for the use of gifts, within the broad category of the original gift; and (3) after a hundred years to make a scheme for the use of the gift for any charitable purpose which may seem expedient. In discussing the lacunæ of a "social service State" Lord BEVERIDGE rightly gives prominence to the needs of age—housing and special homes—and the need for a new approach in the medical treatment of the aged. The British Medical Association committee's report is quoted with approval, with the emphasis on geriatric departments and the possibility of discharge of many of the patients to appropriate accommodation outside the hospital service. "The picture presented in this chapter is a grim one. It is a picture of unhappiness of many different kinds, with relieving agencies working against odds. The unhappiness is not due primarily to want of money; it has not been, and will not be, remedied by redistribution of money." Two practical conclusions emerge: first there must be adequate diversion of physical resources, and secondly the voluntary agencies must have the material resources to enable them to do their work. How they are to obtain these resources in the changed economic and social conditions is "one of the critical problems of the future."

Whether or not Lord BEVERIDGE's more specific recommendations are adopted, there is no doubt of the value of the survey as a corrective to much loose—or should we rather say unpractical?—thinking on the part of those who have believed that responsibility can be shifted to the State and that all will then be well. This tendency in popular thought can be traced in no small degree to the Liberal-Fabian-Socialist school of which Lord BEVERIDGE has himself been such a prominent exponent. That he should now stand back and take stock, and say plainly that the social security for which he has worked is no open sesame, and that voluntary effort

1. Voluntary Action: Report on Methods of Social Advance. London: Allen & Unwin. 1948. Pp. 420. 16s.

Digitized by Google

should be not only tolerated but actively encouraged—is this not perhaps an important turning-point? Are we perhaps standing on a watershed? May we yet hope and expect to see in the years to come a resurgence of voluntary effort, great and small, freed from the slight suggestion of antagonism on the part of the learned and enlightened who mould the thoughts of the younger generation of economists and politicians?

Annotations

INFANT MORBIDITY

EVER since the time of John Graunt, infant health has been the happy hunting ground of the vital statistician. Mortality, whose extent and nature are recorded by law, has because of its accessibility been the measure of child welfare used in innumerable studies. Yet it is morbidity, the precursor of death or serious disability, which is the everyday cause of anxiety to parent and doctor; so more precise knowledge of the incidence of illnesses in infancy, their case-fatality rates, and the chances of cross-infection is certainly required. In an attempt to supply such information, Selwyn Collins,[1] chief statistician to the U.S. Public Health Service, has analysed the results of a series of periodic canvasses of families living in different parts of the United States in the early 1930's. Broadly speaking, the morbidity experienced varied little, and the results have been combined to give a comparison of the age-distribution of the various groups of causes of sickness and death among infants in their first year.

In the U.S.A., as elsewhere, the trend in infant mortality, particularly in the later months of the first year of life, has been consistently downwards; and the death-rates at successive months thus show a sharp decrease with increasing age. Morbidity-rates, on the other hand, decline from a high rate under 1 month to a minimum in the second month and then rise to attain, about the sixth month, a new level which is maintained for the remainder of the year. More specifically, digestive and genito-urinary disorders are remarkable for their high incidence in the first few months of life, whereas the infective disorders, upper respiratory infections, measles, ear diseases, and tuberculosis all have incidence-rates which rise steeply with age. Whether this is due to the fading away of immunity derived from the mother or to the increasing risks of exposure it is difficult to say. Collins gives interesting details of the chances of cross-infection in the various infectious diseases. The risk of an infant being infected by another child in the same household is measured by the secondary-attack rate. Thus whooping-cough not only has a high incidence, particularly in the last six months of infancy, but is so infectious that of 100 infants exposed to a case in the household nearly 100 will become infected. Chickenpox is similar in its high incidence and maximum secondary-attack rate of 75–80%. In measles and german measles the secondary-attack rates are roughly 40%, while mumps, which has also the lowest incidence, never has a secondary-attack rate much above 20%.

The usual hospital and national mortality statistics give no indication of either the prevalence or the case-fatality rates of the illnesses of infancy. Collins's findings, though limited in scope, suggest that the chief causes of illnesses among infants are the common respiratory and digestive diseases, with whooping-cough and ear disease high on the list; but deaths result mainly from congenital and neonatal conditions, pneumonia, and diarrhœa and enteritis. The differences in case-fatality rate thus implied are brought out by comparing the number of illnesses of each type reported in the surveys. Pneumonia, for example, causes 1 death for every 10 reported cases; about 1 in every 25 accidents are fatal; whereas death follows only 1 in 100 attacks of whooping-cough and influenza, and only 1 in 500 cases of measles or ear disease. These are, of course, only rough indications, based on restricted evidence and complicated by the therapeutic innovations of the 'thirties, but the method of relating special morbidity surveys to national mortality statistics is one which we might well emulate.

1. Collins, S. D. *Publ. Hlth Rep., Wash.* 1948, **63**, 69.

GASTRO-ENTERITIS FLYING SQUAD

IN what is believed to be the first venture of its kind in the world, the Hospital for Sick Children, Great Ormond Street, London, has organised a flying squad to go to the help of institutions or others in difficulties over an outbreak of infantile gastro-enteritis. The scheme, which is being partly financed by King Edward's Hospital Fund and has the good will of the Ministry of Health, starts on Nov. 1. The squad will normally consist of up to five fully trained nurses and one doctor, to be taken from the team which has been working on this disease at Great Ormond Street. The primary purpose is, however, not to conduct research but to fill any gap in resources for investigation and treatment; and it is hoped that medical officers of health will use this service. Equipment will be carried in a lorry containing, besides drugs, sterilisers and everything needed for transfusions and infusions. Normally the resources of the nearest laboratory will be used for bacteriological studies; but the lorry also contains a power-driven centrifuge and other apparatus for simple work of this sort. Thus in isolated areas the unit could work independently of any hospital or institution, providing, if need be, a domiciliary service.

The help of the squad, which is prepared to go anywhere, should be sought through the local medical officer of health or regional hospital board, or where the need is acute by telephoning the house-governor at Great Ormond Street (Holborn 9200).

IN THE MINES

AT the best of times mining is a hazardous occupation; and the conditions of the late war, with its shortages of men and materials, and its demand for greater production, were expected to aggravate the risks. This expectation, however, was only partly justified, as Mr. J. R. Felton, the chief inspector, shows in his report for the seven years from 1939 to 1946.[1] The death-rate per 100,000 man-shifts, which was 0·37 in 1939, mounted to 0·46 in 1941, but after that it regressed to 0·30 in 1945 and 1946. Translated into actual numbers, 783 miners were killed in 1939, 550 in 1945, and 543 in 1946. In parallel with the fall in fatalities, the rate of serious injuries decreased from 1·49 per 100,000 man-shifts in 1939 to 1·28 in 1946. Analysis of the 2617 fatal or serious injuries sustained underground in this year shows that 1293 (49%) were caused by falls of ground, 660 (25%) by haulage accidents, 295 (11%) by the use of explosives, 73 (3%) by gases, coal dust, and fires, 63 (2%) by machinery, and 233 (10%) by other causes. Among the factors which, Mr. Felton suggests, may have contributed to this decline are concentration of work in smaller units with larger roads and better supervision; advances in technical knowledge; the more widespread application of principles of roof control and support; greater use of steel supports; inspection; and the education and training of miners. The record of less serious injuries, involving three days' absence from work, is much less satisfactory. The number rose from 134,072 in 1939 to 181,059 in

1. Ministry of Fuel and Power: Report of H.M. Chief Inspector of Mines for the Years 1939–46. H.M. Stationery Office. Pp. 38. 9*d*.

Digitized by Google

1945, falling a little to 167,210 in 1946. The apparent discrepancy between this increase and the downward trend of major accidents is probably explained, says the report, by "factors such as more regular employment during the war years, the incidence of P.A.Y.E., higher rates of compensation benefits, a greater tendency to regard minor accidents more seriously, and the higher average age of the employees."

Discussing the growing preoccupation with dust suppression, the report cites the South Wales area, where by the end of 1946 almost 600 miles of steel water-pipes had been installed underground for this purpose. The report also refers to first-aid arrangements as often unsatisfactory, usually for the reason that no suitable person is in charge; septic infection of minor injuries—still common, though less of a problem than formerly—could be reduced with better equipment and more highly trained personnel. In point of fact a scheme for the erection and expert staffing of treatment centres at mines was initiated towards the end of the period under review. The concession, arranged in 1944, by which trained first-aid workers may administer morphine in emergency, has proved to be a wise one.

STREPTOMYCIN RESISTANCE AND DEPENDENCE

IN talking loosely of organisms developing resistance we lay ourselves open to a charge of Lamarckism, for the resistance is not developed but unmasked. It is now clear that the appearance of strains of tubercle bacilli or other organisms resistant to streptomycin results from selection of naturally occurring hereditary variants. When streptomycin is added to a culture of organisms, either in the body or in the laboratory, a culture medium is formed which is selective for the growth of resistant variants. The facts that these resistant organisms are usually genetically stable and are present only in small numbers in a random population support the view that they are produced by mutation regardless of the presence of the drug. But how can we explain that some strains of organisms require streptomycin for growth? Miller and Bohnhoff [1] obtained a streptomycin-dependent strain of meningococcus, and Paine and Finland [2] have found streptomycin-dependent variants of staphylococci and coliform organisms. Spendlove and his colleagues [3] have described a strain of *Mycobacterium tuberculosis* which grows much better when streptomycin is added to the culture medium; this strain was isolated from a patient whose infection progressed rapidly during streptomycin therapy.

The full explanation of streptomycin dependence and resistance must necessarily await understanding of the mechanism by which the drug exerts its antibacterial effect. Dependence on streptomycin appears to be much more labile than resistance, but Paine and Finland point out that dependence and resistance may be closely related traits. They found that both sensitive and dependent organisms were present in the same predominantly dependent colony which appeared after the initial exposure of a sensitive strain to the antibiotic. Under appropriate conditions dependent variants gave rise only to sensitive organisms, and the same concentration of streptomycin that completely inhibited the growth of the parent sensitive strain was necessary for the growth of its dependent variant. If streptomycin acts by blocking an essential metabolite or enzyme system, then it seems more than coincidence that the concentration of drug which inhibits the sensitive strain should also make for growth of the dependent variant. In the latter the original essential metabolite may be replaced by some part of the streptomycin molecule which closely resembles it. In the resistant variants an alternative mechanism may function in place of the metabolite or enzyme system that is blocked by streptomycin in the sensitive strain. As Paine and Finland point out, both dependent and resistant variants grow much more slowly than their parent sensitive strain, and this may be why streptomycin-resistance is often not encountered until late in a course of treatment.

1. Miller, C. P., Bohnhoff, M. *J. Bact.* 1947, **54**, 467.
2. Paine, T. F., Finland, M. *Ibid*, 1948, **56**, 207.
3. Spendlove, G. A., Cummings, M. M., Fackler, W. B. jun., Michael, M. jun. *Publ. Hlth Rep., Wash.* 1948, **63**, 1177.

ASIATICOSIDE IN LEPROSY

THE small umbelliferous plant, called *Centella asiatica*, or Indian pennywort, has been a traditional Indian remedy for leprosy and syphilis. About three years ago French workers in Madagascar reported that asiaticoside, a preparation obtained from the plant, was of some use in human tuberculosis. The drug is a white tasteless crystalline powder, insoluble in water, though it can be made soluble by oxidation with potassium permanganate. No further information on the subject appeared at the time, and we understand that some in-vitro tests of the drug in this country against *Myco. tuberculosis* were disappointing. Two French workers, Boiteau and Saracino,[1] have now reinvestigated the therapeutic possibilities of asiaticoside and claim that it is of considerable value in the treatment of leprosy and lupus erythematosus in man and of experimental tuberculosis in the guineapig. Without giving the number of cases treated, they mention remarkable results obtained in a Madagascar leprosarium. All forms of leprosy—lepromatous, neural, and tuberculoid—are said to have shown clinical and symptomatic improvement, and the causal organism, *Myco. lepræ*, disappeared from mucous lesions within a fortnight. Eight of the lupus cases were treated with asiaticoside by intramuscular injection. The first few injections apparently produced an exacerbation of the lesions, which finally cleared and underwent epithelisation after two months' treatment. The drug appears to be relatively non-toxic, the only side-effects noted being a slight fall in blood-pressure and a heavy feeling in the limbs.

In view of the legion of remedies for leprosy that have not stood the test of carefully controlled observation, comparative studies should be made in the treatment of leprosy with asiaticoside and with sulphones such as 'Diasone' and 'Sulphetrone,' which seem to be the drugs of choice at the moment.

THE BALLISTOCARDIOGRAM

LYING in bed, some people are uncomfortably aware, particularly with overaction of the heart through emotional disturbance or after stimulating drugs, that with each heart-beat their whole body moves. Actually movements of this sort take place in all of us, and their nature and extent can be measured by getting the subject to lie on a table or bed suspended so that the motion is transmitted to fluid in a manometer. Alternatively, the movements can be converted with a high-frequency oscillometer into voltage changes, which are recorded optically. The apparatus used for making this record, known as a ballistocardiogram, has been described by American workers.[2] According to Starr and Mayock,[3] the normal ballistocardiogram has four main waves, which synchronise with ventricular systole, and smaller and more variable waves in diastole. They suggest that an abnormal ballistocardiogram indicates disease or some alteration in dynamics of the heart, as in hyperthyroidism or hypertension; and though admitting that an abnormal record has been obtained in the absence of detectable heart disease, they deny that any but a normal curve is ever obtained in a healthy young adult. One positive

1. Boiteau, P., Saracino, R. *Méd. franç.* 1948, **8**, 251.
2. Nickerson, J. L., Curtis, H. J. *Amer. J. Physiol.* 1944, **142**, 1. Brown, H. R. jun., Pearson, R. *Amer. Heart J.* 1948, **35**, 756.
3. Starr, I., Mayock, R. L. *Amer. J. med. Sci.* 1948, **215**, 631.

Digitized by Google

observation is the finding of a distinctive curve with left ventricular aneurysm. The ballistocardiogram has also been used for measuring cardiac output[3]; indeed Nickerson and his associates claim that this technique is just as accurate as one based on right atrial catheterisation.

ORDINARY GIRLS

ALL girls are silly and ignorant, pronounced Mr. Bennet, without stopping to reflect that all he had done for his own five was to give them a silly mother and precious little education. Small wonder if they were occupied with thoughts of early marriage; and was this, after all, such a bad thing to think about? The "ordinary girls" in Miss Pearl Jephcott's study, *Rising Twenty*,[4] are in much the same position as the Miss Bennets and the Miss Dashwoods of a century ago. They are filling in time until they marry, and filling it with something more useful, on the whole, than drawing, purse-netting, and singing to the harp. Miss Jephcott's study, made in 1945–46, covers just over a hundred such girls, living in three parts of England—a pit village in County Durham, a cluster of blitzed streets near Piccadilly Circus, and a northern industrial town. They were all over 17 and under 21 when she knew them, and they talked to her of their life since they left school—"those years between 14 and 18 when, according to the stock statement which so many made, 'I learnt more than I ever did before.'"

They worked in shops and factories, and nearly all found their work boring. Life begins for them when work finishes, and they are free to spend their evening dancing, skating, or at the cinema, at first with a group of other girls and boys, and later in couples, each girl taken—and paid for—by the boy with whom she is "going steady." But this behaviour does not really justify the accusation, so often made, that these girls are "pleasure-mad." Once they get engaged they settle down quietly enough, and save up for a home. When their betrothed husbands were absent in the Army, many of the girls hardly went out at all. Marriage is their career, and almost the only career open to them which has creative aspects; and the single-mindedness with which they pursue their end would earn them praise if they were students working their way through college. They are not unaware of the heavy obligations of marriage, for they see them borne by their own parents; and some even comment on married life as "all drudgery." Nevertheless it is traditional that they must enter it, and to remain unmarried is to fail. Seen from this angle, their behaviour is perfectly logical and not at all unworthy. They must meet their future husbands, and the accepted way to do this is to go dancing. Youth clubs do not offer comparable opportunities, because there the boys are contemporaries—too young for mates and too rowdy for companions. The cinema sets their standards in appearance and hairdressing, and has on the whole been responsible for a great advance in both since the turn of the century. In the factory the girls are given dull repetitive jobs, entailing long hours of standing. Nursing, which might, if it offered more freedom, prove an attractive alternative, they reject because they believe it would ruin their prospects of marriage. They prefer the boredom and fatigue of a dead-end job because it gives them the money and leisure for their more serious duty of finding a mate. By social and biological standards they are serving the race, and doing it entirely at their own expense.

The tragedy which appears in this study is their paucity of other interests: they are not politically informed, and often fail to join a union; they chiefly read love stories, and they have few constructive hobbies. "The girl who consistently tries to sing, or to dressmake, or to act, or to play a game, let alone to pursue anything a shade more out of the ordinary than any of these, is the exception." Marriage brings them new experience and skills, but debars them still more firmly from interests outside the home. Yet, limited as they are in outlook, these girls, Miss Jephcott finds, are fundamentally good-hearted and kindly. They take their share of the family responsibility, often giving up one or two evenings or an afternoon regularly every week to mind the baby or help with washing or housework. In a world with little attention to spare for the simple business of living they are, in a sense, holding to fundamentals; if they need rescuing—which seems uncertain—it is from the boring circumstances in which they carry out their purpose. Any attempt to help them—whether on the part of youth organisations, churches, educational bodies, or juvenile employment bureaux—should be directed towards enriching their lives.

SYMPATHECTOMY AND THE HEART

IT is well over eighty years since von Bezold demonstrated the rôle of the vagus; but other factors controlling heart-rate have been worked out only recently, and even now the mechanism in man is somewhat obscure. Cardioaccelerator nerves are generally believed to reach the heart through the 2nd–5th dorsal ganglia of the sympathetic nervous system; and Smithwick and his colleagues[1] report that bilateral removal of these ganglia is followed by slowing of the rate, whose response to exercise becomes less pronounced. The effect of unilateral removal is variable; and it seems that, though the sympathetic innervation from the right side usually exerts a greater influence than that from the left, the only way to ensure slowing is to perform sympathectomy on both sides. Two further observations are of interest. First, in a child aged 15 years, bilateral excision of the 2nd and 3rd dorsal ganglia for hyperhidrosis caused "decided diminution" in pulse-rate and a lessened response to exercise; but the same operation in a woman of 56 with Raynaud's disease had no such effect. Secondly, in a group of four hypertensive patients in whom extensive splanchnic denervation had previously been performed without effect on the heart-rate, subsequent removal of the 2nd–5th dorsal ganglia was followed by definite slowing.

The variable response to unilateral sympathectomy is ascribed by Smithwick and his associates to normal variations in sympathetic innervation. Another explanation which cannot be altogether discounted is that, as in the dog, cardioaccelerator fibres may be carried in the vagus; and this would explain the occasional case in which bilateral sympathectomy has little appreciable effect. The practical implications of this work are not altogether clear, but it suggests that in the surgical treatment of hypertension low dorsal sympathectomy, which is liable to result in increased heart-rate, should be accompanied by removal of the 2nd–5th dorsal ganglia. Possibly this operation might be useful also in some cases of angina pectoris accompanied by tachycardia, but careful assessment would first be necessary. From the U.S.A. have come repeated accounts of a "sympathetic syndrome," characterised by headache, precordial pain, tachycardia, and hyperhidrosis; here, too, a localised upper dorsal sympathectomy, despite its risks, might occasionally be justified.

WE regret to announce the death of Dr. C. M. WENYON, F.R.S., on Oct. 24, at the age of 70. Till 1944 Dr. Wenyon was director-in-chief of the Wellcome Research Institution.

3. Cournand, A., Ranges, H. A., Riley, R. L. *J. clin. Invest.* 1942, **21**, 287. Nickerson, J. L., Warren, J. V., Brannon, E. S. *Ibid*, 1947, **26**, 1.
4. London: Faber & Faber. 1948. Pp. 200. 8*s*. 6*d*.

1. Chapman, E. M., Kinsey, D., Chapman, W. P., Smithwick, R. H. *J. Amer. med. Ass.* 1948, **137**, 579.

Digitized by Google

Special Articles

REHABILITATION IN INDUSTRY

L. W. PLEWES
M.A., M.D. Toronto, F.R.C.S.E.
CONSULTING ORTHOPÆDIC SURGEON

JOHN N. BARRON
M.B. N.Z., F.R.C.S.E.
CONSULTING PLASTIC SURGEON

A. R. THOMPSON
M.D. Lond., D.P.H., D.I.H.
CHIEF MEDICAL OFFICER

H. H. NEWELL
REHABILITATION SUPERINTENDENT

VAUXHALL MOTORS LTD., LUTON, BEDS

THERE is growing awareness of the urgent necessity of conserving the nation's man-power; and though the prevention of disablement, as well as the employment of disabled people, can make a contribution to this end, it is in industry itself that a solution of the present wastage can be found.

As a result of encouragement by an enlightened directorate, a community of 12,000 people engaged in the medium engineering industry of motor-vehicle manufacture now enjoys its own domestic rehabilitation centre. For its foundation we acknowledge the help and guidance of the pioneer organisation at Austin Motors.

A rehabilitation team has been set up consisting of consulting orthopædic and plastic surgeons, an industrial medical officer, a rehabilitation superintendent and his deputy, and an industrial physiotherapist. The activities of this team, in group consultation, are centred in a special rehabilitation machine shop, or "retraining shop," run on standard production lines and accommodating up to 60 men. The scheme has been in operation since 1945, and the shop opened in April, 1946.

The shop is housed in a new building set in pleasant surroundings, and features such as good lighting and interior decoration have been the subjects of special study. Here, by utilising standard machines, or bench work, modified and adapted to secure controlled range and power of movement, remedial occupations and graded work are prescribed for patients by the visiting surgeons and the industrial medical officer.

The full team visits once a week, when, at a follow-through clinic and during a subsequent round of the retraining shop, all patients are reviewed, treatment is discussed, and progress is recorded.

A whole-time rehabilitation superintendent is in charge of the retraining shop. He is a trained engineer of senior status who, before taking up his duties, was given an opportunity of studying the broader social and economic aspects of the local industrial conditions and hospital services. He is responsible to the company medical officer, and his duties include the placement of all incapacitated factory personnel. He is the liaison officer between the hospital and the factory.

An assistant rehabilitation officer, selected for his abilities as a teacher of machine-shop practice, is in immediate charge of the men in the retraining shop, and his services are available if vocational training is required.

Though the scheme is intended primarily for works accident cases, disabled ex-Servicemen and employees injured away from work are catered for. The report of the Delevingne Committee showed that industrial accidents accounted for only 30% of the total; hence there is ample opportunity for rehabilitation within industry apart from purely works accident cases. Medical and psychological cases presenting difficulty in placement are also admitted for graded work until they can be accommodated elsewhere in the factory.

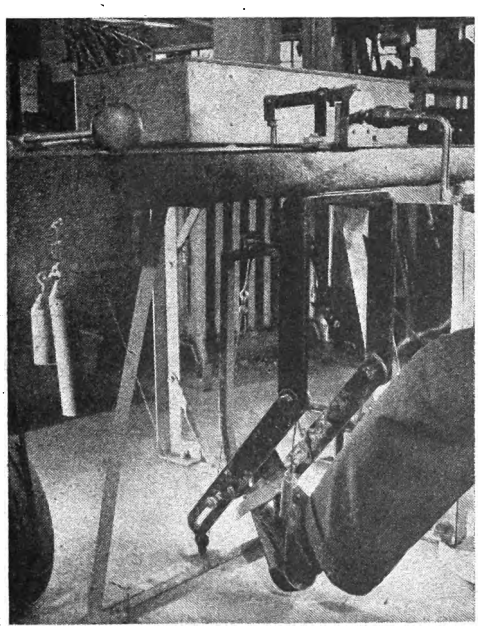


Fig. 1—Development of quadriceps muscle against graduated counter-weights at a leg-operated bench for a countersinking operation.

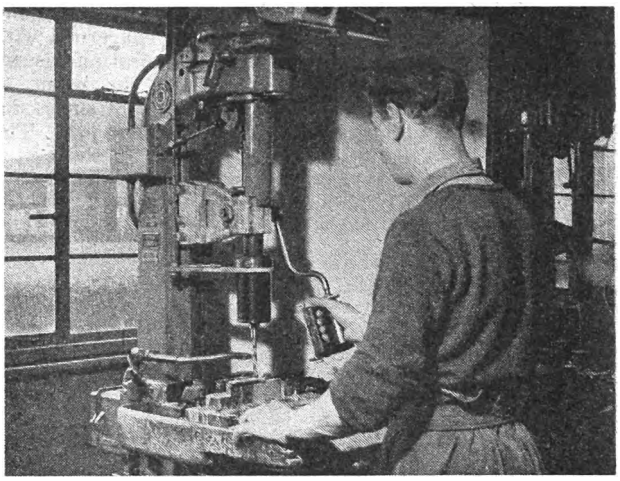


Fig. 2—Combined active and passive flexion of the fingers using a 'Sorbo'-padded and adjustable grip attached to the handle of a single-spindle drilling machine. This patient was successfully treated after primary suture of cut flexor tendons of three fingers.

In the twenty months after the shop was opened, some 452 patients passed through it. Of these, 355 (78·6%) were surgical, 72 (15·9%) medical, and 25 (5·5%) psychological. The average length of stay for all patients was thirteen weeks, and that for surgical cases six weeks. In some instances placements were preceded by a temporary trial period on selected work within the factory to ensure that the work was suitable to the patient and that the patient was acceptable to the supervision. In this connexion emphasis is placed on finding the right job rather than a light job, but in no sense is the retraining shop regarded as a refuge for invalids, and the general morale of the men has remained consistently high.

Summary of admissions

Works accident cases	257(57%)	Medical cases	72(15·9%)
		Surgical cases	355(78·6%)
Non-occupational cases	195(43%)	Psychological cases	25(5·5%)
Total	452		

Surgical cases

Fractures	125(35%)	Soft-tissue injuries	230(65%)

Disposal

Return to full work	382(85%)	Return to modified work	70(15%)

In addition to the cases which passed through the shop, some 450 other placements made necessary by health

Digitized by Google

reasons were dealt with by the medical and rehabilitation departments.

PRINCIPLES

The patients or "retrainees" are paid the equivalent of their basic rates of pay plus 20% in lieu of bonus where this is applicable. Suitable work is selected from within the factory and scheduled for the shop. Much of this work is familiar to the men, and their contribution to the production demands of the factory is in our view a far more powerful stimulus to recovery than is the standard type of occupational therapy. Moreover, the advantages of working in a "live" shop where treatment is individually planned, and with a forward outlook on recovery, are of immense value, both from the economic and psychological points of view, in securing the patients' full coöperation.

One of the principles underlying the establishment of this scheme is the value of repetitive exercise, and much of the research that is going on is concerned with the adaptation of machinery so that its operation ensures controlled repetitive movement. From the point of view of the injured workman the criterion of successful treatment is his ability to do his pre-accident job. The

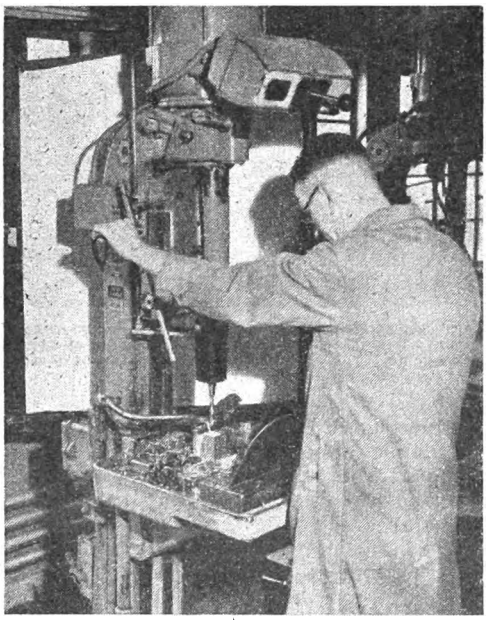


Fig. 3—Mobilisation for fractured shoulder-joint with adjustable grip transposed from right to left side of single-spindle drilling machine.

surgeon's aim should be the maintenance or development of coördinated full muscle power across joints capable of their normal range of movement in limbs which have normal sensation. Viewed from this angle, the actual surgical procedure, reduction of fractures, suturing of tendons, and draining of felons, though essential, is merely the gateway to the path of recovery.

There are four causes of loss of limb function from trauma: direct severance of vital structures, tissue destruction by infection or by burning, cicatricial replacement of lost tissues or of œdematous exudates, and artificial immobilisation. In all of these the important factor militating against recovery is the time during which function is depressed or prevented, and thus the effects of all may be considered in terms of partial or total immobility. It is well recognised that there are certain therapeutic indications for rest, but these indications are far less common than has been believed in the past. This leads us to review all injuries to reduce immobilisation to the minimum and to encourage function in all structures which do not demand rest. One of the most noticeable features in a régime of this sort is the

Fig. 4—Development of quadriceps by pedal-action press. This brake-shoe riveting machine gives 10,000 movements a day and is adjustable for range and power of movement at knee-joint.

absence of circulatory disorders. An active circulation is reflected in the rapid healing of bone and soft tissues, with a consequent reduction in joint stiffness and loss of muscle tone. The restoration of maximum function depends on the maintenance of such muscle power and movement as is possible after injury and the re-education of such function as is lost. It is in this process of re-education that repetitive exercise is the keystone, and it is just as true that practice makes perfect in post-accident treatment as it is in the acquisition of any other skilled procedure. The development of muscle power, of range of movement, and of coördination can most readily be effected by repeated attempts to improve what is already there.

This treatment requires careful control to prevent fatigue; so repetitive exercise should be alternated with repetitive rest. It requires control also to ensure that not only are all the normal functions being maintained at a normal level but also that re-education is proceeding without the development of abnormal or "trick" movements.

Fig. 5—Pipe-bending over a former, of special value in most forearm and hand injuries for maintaining muscle tone both during and after immobilisation in plaster.

Digitized by Google

Under these conditions men can work their way back to normal in surroundings with which they are accustomed, fully employed on a constructive job, with the stress on a system of treatment which they know can lead them back to their pre-injury status.

INDUSTRIAL OCCUPATIONAL THERAPY

For the provision of remedial movements highly skilled operations are completely unnecessary. By far the most valuable machine-tool is the single-spindle drilling machine. By adding special equipment to the operating lever most movements can be obtained for hands, arms, and shoulders. Other exercises for upper limbs are provided by the bending of copper and steel pipes round formers at the bench. Bending a $^3/_8$ in. steel rod by pulling on a 5 ft. bar gives an easy rowing motion which promotes development of the main trunk muscle groups. By adjusting the height of the lever on the machines controlled range and power can be obtained for arm and shoulder injuries. Simple bench vices operated by the foot are valuable in the early treatment of ankle and knee injuries. More intensive muscle development is encouraged on kick and pedal action riveting machines used in the closing of small tubular rivets. On such machines it is possible to obtain 9000–10,000 movements daily without fatigue. Fly presses, lathes, and milling machines make up the standard equipment, and besides these there are special pieces of apparatus capable of normal production work which

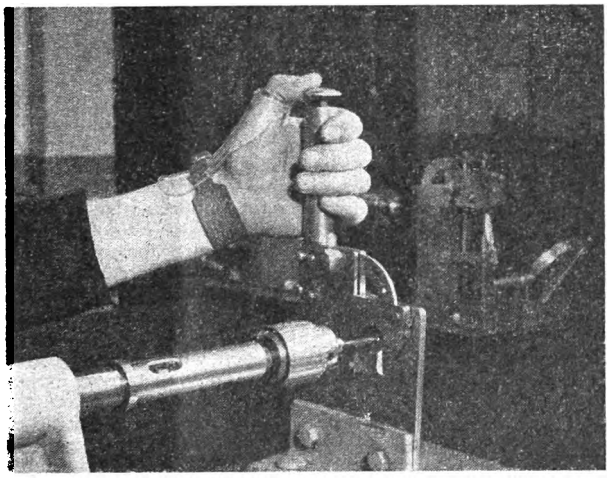


Fig. 6—Spring-loaded plunger incorporated in a hand tapping device to encourage flexion of thumb-joint after suture of tendon. Trick movements by the thumb adductors are prevented by the moulded 'Perspex' splint.

have been designed from anatomical blueprints for specific therapeutic purposes. The ideas for appliances and adapters to suit individual patients arise from consultation between the surgeon and the engineer. These conferences are of great mutual benefit to both sides, who learn much about the principles and problems of each other's profession. "Retrainees" are encouraged to suggest modifications of any appliance or machine that would still further aid recovery, and some of these suggestions have evolved into standard remedial apparatus. The services of the more highly skilled men and suitable psychological cases are utilised in the design and construction of appliances required in the shop.

A wide selection of dry bench work which can be graded for dexterity, range of movement, and power is found invaluable in the early stages of hand and arm injuries. This work is suitable even for infections and fractures of the hand which require dressings and splints, and there are few patients who cannot thus be accommodated within a day or two of injury.

TABLE I—PERIODS OF INCAPACITY AFTER COMMON LESIONS

Diagnosis	Vauxhall patients 1945–48 (accident and non-works accident cases)			Other patients 1945–48 (Luton and Dunstable Hospital fracture clinic)			F.C.R. (1)	F.C.R. (2)
	No. of cases	Average days off work	% losing no time	No. of cases	Average days off work	% losing no time (1945–46)	Average days off work	
Pott's fracture.. ..	39	18·9	15	132	32·9	2	329	77
Colles's fracture ..	17	3·9	80	59	22·4	10	203	49
Fractured scaphoid ..	30	7·7	72	55	14·7	30	322	77
Fractured hallux ..	26	5·0	54	16	24·5	10	..	..
Operations for internal derangement of knee	12	16·25	..	20	31·5	..	..	..

F.C.R. (1) B.M.A. Fracture Committee report, 1935. Cases not treated in organised fracture clinics.
F.C.R. (2) B.M.A. Fracture Committee report, 1935. Cases treated in fracture clinics of Liverpool and Manchester.

Continuity of treatment and of observation is assured under these conditions up to the time for return to full work. Every aspect of the patient's welfare is covered, and his absorption back into the normal working community is made as rapidly and smoothly as possible.

Cases requiring further investigation, radiography, or plaster changes at the hospital are collected once a week and, in company with the rehabilitation superintendent, are transported to and from the hospital by coach with considerable saving of time. During these visits the superintendent can make personal contact with new patients still actually in hospital, and by means of a follow-up system the more serious cases can be assured of an early inclusion in the retraining scheme.

One of the by-products of successful rehabilitation is the number of man-hours saved to the benefit of the patient, to industry, and thus to the community as a whole. Tables I and II, give some indication of the results to be expected in some of the commoner injuries encountered in industry.

PHYSIOTHERAPY

It is obvious that physiotherapy is a necessary and important adjunct to an industrial project of this kind. Here there is a modern well-equipped unit employing a whole-time staff. It is situated close to the retraining shop, and this proximity suggests the importance attached to the close coöperation between them. From the physiotherapeutic point of view it must be admitted that the ability to rely on long periods of controlled active exercise in the shop ($42^1/_2$ hours a week) is a great advantage. On the other hand, orthodox physical treatment is found necessary in 60% of cases under the following group headings:

(1) *Re-education of Movements to a Point where they can be Utilised Actively at Work.*—In this group come, for example,

TABLE II—PERIODS OF INCAPACITY AFTER HAND INFECTIONS APRIL–DECEMBER, 1947

Diagnosis	Vauxhall patients			Other patients		
	No. of cases	Average days to no growth	Average days off work	No. of cases	Average days to no growth	Average days off work
Paronychia ..	6	7·1	3·8	42	6·6	5·5
Pulp infections ..	14	6·0	5·0	66	9·7	11·9
Subcutaneous whitlow	8	5·7	5·5	30	6·0	4·5
Web-space infections	6	2·6	6·1	21	7·6	8·7

Digitized by Google

many of the hand injuries, joints released from splints, sutured tendons, and rested muscles. For these the "feeling of movement" is re-educated under supervision. This is a delicate and skilled matter, and should not be entrusted to the coarser persuasion of mechanical assistance obtainable from adapted machinery.

(2) *Maintenance and Stimulation of the Circulation.*—Here the various forms of heat treatment and massage are invaluable. In the early stages of many upper-limb injuries a persistent sympathetic constrictor effect must be combated, especially in cold weather. These cases arrive at the factory in the morning with cold blue hands incapable of working efficiently. Fifteen minutes in the high-temperature wax bath releases the spasm and mobilises the limb to a point where its own activity on the production line maintains its circulation throughout the day.

(3) *Muscular Disorders.*—Muscle sprains and ruptures, fibrositis, and tenosynovitis form a large group which requires physiotherapy as a primary treatment. This is given while a patient is employed in selected or modified occupations which may or may not necessitate admission to the shop. Many of these patients are absorbed back into the factory where the demands made on them are checked by the rehabilitation

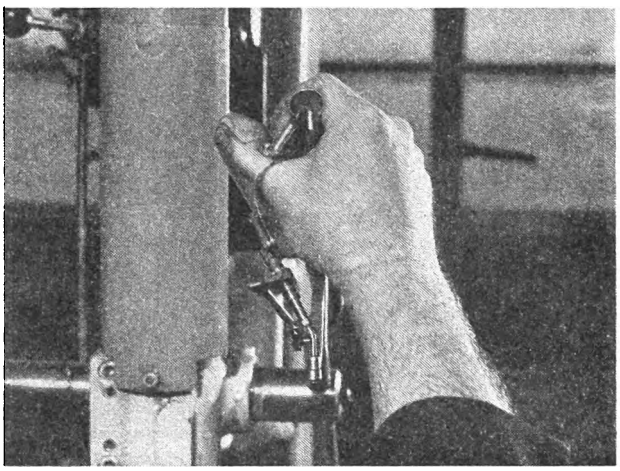


Fig. 7—Mobilisation (adduction and abduction) of thumb by grip attached to handle of drilling machine operated by squeezing action.

superintendent so that progress is not retarded by enforcement of unsuitable work.

(4) *Infections.*—Cases of chronic sepsis, osteomyelitis, and unhealed wounds in the later stages of treatment attend for either short-wave or ultraviolet therapy.

(5) *Nerve Injuries.*—Whereas the shop can take care of non-paralysed muscles, special attention should be paid to denervated muscles to prevent wasting, contracture, and deformity. The full resources of the physiotherapeutic department are necessary to obtain maximal recovery of function.

The demand made on this department was as follows:

Therapy	*Percentage of cases treated*	*Indication*
Exercise ..	26·0	Early re-education of movement in tendon and joint injuries, fractures, burns, and splinted limbs.
Short-wave ..	18·5	Infections, tenosynovitis, and chronic osteomyelitis.
Wax baths ..	17·0	Healed hand injuries.
Infra-red rays..	10·0	Pre-wax-heat therapy.
Faradism ..	9·5	Re-education of intrinsic hand muscles.
Massage ..	9·0	Fibrositis, tennis elbow, and scars.
Ultraviolet rays	8·5	Chronic wounds and general tonic therapy.
Galvanism ..	1·5	Nerve injuries.

MEDICAL REHABILITATION

Because the emphasis has been on the treatment of surgical conditions, the problem of medical rehabilitation has been thrown into greater relief. An attempt is being made to study the effects of graded work and controlled

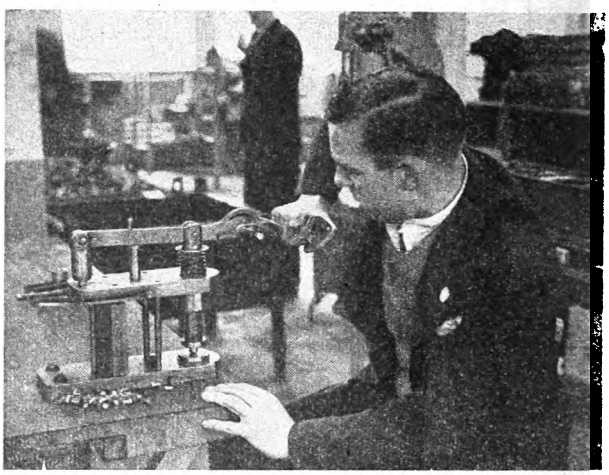


Fig. 8—Spring-loaded hand press for mobilisation of wrist in later stages of recovery from fractured scaphoid, Colles's fracture, &c.

environment on groups of medical cases which can be briefly considered under the following headings:

(1) *Convalescents from acute illnesses* have responded very well to a period of graded work before their return to full activity. Evidence of this is the fact that most of them gained in weight while in the retraining shop, but restored earning capacity after protracted illness was no doubt a contributory economic factor.

(2) *Peptic-ulcer cases* remained quiescent in symptoms, kept good time, and required no special treatment beyond facilities for a light midday meal and relief from night work. It is not suggested that such a régime would solve the problem of the chronic dyspeptic in industry, the solution of which is still far to seek.

(3) *Cases of industrial dermatitis* settled down quickly on dry clean work and were submitted to trial periods in contact with the suspected cause to test their skin reactions.

(4) *Chronic medical cases*, in particular those associated with advancing age and inability to compete with younger men, responded less satisfactorily, and little or no material advantage followed attempts at rehabilitation on graded work. In our view this type of case calls for suitable and permanent placement rather than for admission to an industrial rehabilitation centre.

(5) *Cases of neurosis* responded in a variable manner. Mild anxiety states with or without depression, whether precipitated by domestic or working conditions, improved provided they were of recent origin, when given a period of relief from the hectic atmosphere of the production line. Others associated with simple or chronic industrial fatigue, maladjustment, or resettlement difficulties after war service responded favourably though some required occupational adjustment on discharge.

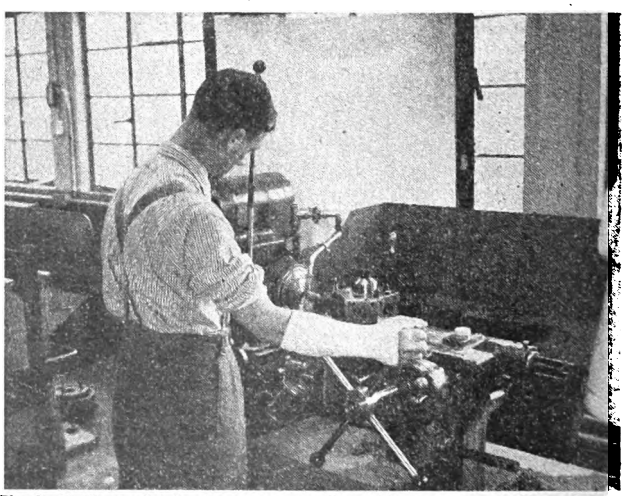


Fig. 9—Patient with fractured scaphoid working a capstan lathe with his forearm in a plaster splint modified to allow maximal function of hand and arm.

Digitized by Google

In all these cases diversional therapy, such as the construction of remedial appliances, was found to be most beneficial.

CONCLUSIONS

Our experience leads us to believe that, where facilities are provided for comprehensive rehabilitation within industry, the injured employee needs little or no persuasion to avail himself of this service. Such a service has an important contribution to make towards social medicine and produces good relations between the worker and his employer and with the medical profession as a whole.

Certain aspects of the scheme can be expanded into a service designed to deal with the accident problem of a composite community.

Group industrial rehabilitation centres should be based on up-to-date and well-staffed hospitals where facilities for diagnosis and controlled surgical treatment are present.

The hospital should be supported by an enlightened service of general practitioners who would be prepared to modify present methods of certification and accept new standards regarding fitness for modified or selected work. Training in the basic principles should form part of the medical school curriculum.

Attached to the hospital there should be a remedial workshop with facilities for general exercise therapy. This should be closely allied with the physiotherapy department and should be supplied with equipment and work from the local industry.

The equipment should be of a simple nature in which the principles of adaptation can be applied and studied. The work done should be constructive, interesting, and involve repetitive movement.

Patients treated in the workshop should be limited to those who cannot be absorbed back into suitable conditions in their own industry.

Liaison with all industrial interests of the district should be created by a rehabilitation superintendent working from the hospital. His responsibility should be detailed job-analysis in all accident cases and survey of the patients' working environment so that gradual return to full employment can be expedited by a wise choice of interim occupation during the retraining period. He should also superintend the workshop.

Such a group centre is already in existence at the Luton and Dunstable Hospital, where it has been encouraging to find that the support from industry has been most generous, and that the coöperation from management, supervision, and the workers leaves nothing to be desired.

ACADEMIC SALARIES

As soon as the Government accepted, in principle, the recommendations of the third Spens Committee it became obvious that universities would have to review their remuneration of doctors holding academic posts. Such a review might have far-reaching consequences for university salaries as a whole, and the difficulties raised are serious. On the medical side the Royal College of Physicians, expressing grave concern, has recommended that "the remuneration of whole-time academic appointments should be brought into appropriate relationship with that of other consultants and specialists," which it thinks "might be done by additional remuneration for hospital responsibilities." But it also trusts that "careful attention will be given to the remuneration of academic staffs engaged in the fundamental sciences, so that their position will not be prejudiced." Its resolutions have since been endorsed by the council of the Royal College of Surgeons, in whose annual report they are now published.

Dr. Charles Hill, for the B.M.A., has pointed out that "for the first time we have ranges of remuneration accepted by the Government as appropriate to large sections of the profession and we shall seek their proper application to groups not specifically covered by the two Spens reports."

Public Health

HOME NURSING OF PREMATURE BABIES IN NEWCASTLE-ON-TYNE

F. J. W. MILLER
M.D. Durh., M R.C.P., D.C.H.

From the City Health Department and the Department of Child Health, Royal Victoria Infirmary, Newcastle-on-Tyne

THE object of this study has been to discover the results of nursing and treating premature infants in their own homes and to collect information to answer the question whether it is better for a premature infant to be born at home and nursed there or to be admitted to hospital. The facts presented here were obtained in 1945–47 after the introduction of the notification of prematurity and the establishment of a home-nursing service for the care of premature infants. The methods used have been previously described.[1]

The background of this experience is an industrial city of 280,000 inhabitants in north-eastern England. The standards of housing have always been low but were much improved by strenuous municipal effort in the 1930's. The Overcrowding Census in 1936 showed that 10% of working-class families lived in overcrowded conditions (calculated on a basis which did not include any children under the age of one year in the permitted number for a room). Since 1939 economic standards have improved, housing conditions have deteriorated, but the infantile mortality has fallen steadily from 91 in 1937 to 40 in 1945 and 41 in 1946.

TABLE I—INCIDENCE OF PREMATURITY

Place and date	No. of births	No. of premature births	No. of live births	No. of live premature births
Newcastle-on-Tyne 1945–47 ..	16,323	1042 (6·4%)	15,862	916 (5·7%)
Birmingham [3] 1943–46 ..	85,305	5939 (6·9%)	83,118	5006 (6·0%)

In this country and in America most of the estimates of the incidence of prematurity have been made from hospital data. These vary between 3% and 12%. Baird [2] quotes Bundesen as stating the incidence of prematurity in Chicago as 6·5%. In Newcastle the incidence in 1945–47 was 6·4%, a figure almost the same as that published for Birmingham [3] (table I).

The weight distribution of the 916 infants was as expected: 54% of the premature infants were between $4^1/_2$ and $5^1/_2$ lb. at birth, 27% from $3^1/_2$ to $4^1/_2$ lb., and 19% $3^1/_2$ lb. or less.

The neonatal mortality again showed the well-known facts: of the 916 infants 208 (22·8%) died within the first twenty-eight days. Almost two-thirds of these, 124 (59·6%), died on the first day, and 188 (90·4%) in the first week.

In 1945-47 there were 400 neonatal deaths in Newcastle; 208 (52%) were in premature children.

RESULTS OF HOME NURSING

The fate of children born at home and in hospital in the first twenty-eight days is shown in table II. These groups cannot be directly compared, but the numbers and results are equal until the weight-group $4^1/_2$–$5^1/_2$ lb. is reached, where, in my opinion, the difference is likely to be the result of different obstetrical rather than pædiatric care.

1. Miller, F. J. W. *Arch. Dis. Childh.* 1947, **22**, 54.
2. Baird, D. *J. Obstet. Gynæc.* 1945, **52**, 217, 339.
3. McNeil, C., Crosse, V. M., Hallum, J. L. *J. R. sanit. Inst.* 1947, **67**, 403.

Digitized by Google

TABLE II—DEATHS IN FIRST 28 DAYS IN VARIOUS WEIGHT-GROUPS AT HOME AND IN HOSPITAL, 1945–47

Weight	Home group		Hospital group	
	Births	Deaths	Births	Deaths
Under 2 lb. 8 oz. ..	36	35 (97%)	33	33 (100%)
2 lb. 9 oz. to 3 lb. 8 oz.	52	32 (61·5%)	53	35 (66%)
3 lb. 9 oz. to 4 lb. 8 oz.	124	22 (17·8%)	117	23 (19·6%)
4 lb. 9 oz. to 5 lb. 8 oz.	167	14 (8·4%)	334	14 (4·2%)
All weights ..	379	103 (27·2%)	537	105 (19·5%)

Table III shows the results in home care for the first twenty-eight days. Just as a direct comparison of home and hospital births cannot be made, so it is impossible to compare directly the "specialled" and "not specialled" groups. We could not provide, during this period, special care for all premature infants born at home, and medical practitioners and district midwives called for assistance from the "premature infant" nurses at their own discretion. In general, special assistance was asked for if they thought the smallest infant might survive or the larger infant ($4^1/_2$–$5^1/_2$ lb.) gave rise to anxiety. The results, however, merit note, especially in the group of infants between $3^1/_2$ lb. and $4^1/_2$ lb., in which there were only 7 deaths among 82 infants specialled, and only 22 deaths among 124 premature infants in the whole city.

ASSESSMENT OF RESULTS

To answer in any strict mathematical sense the question whether it is better for a premature infant to be nursed at home or to be removed to hospital, it would be necessary to make a comparison between the results of the treatment of a large group of premature children born and nursed at home with the results in a group of similar composition born at home under similar

TABLE III—RESULTS OF HOME CARE OF PREMATURE INFANTS FOR FIRST 28 DAYS, 1945–47

Weight	"Not specialled"			"Specialled"		
	Total	Living	Dead	Total	Living	Dead
Under 2 lb. 8 oz. ..	28	1	27	8	..	8
2 lb. 9 oz. to 3 lb. 8 oz.	27	7	20	25	13	12
3 lb. 9 oz. to 4 lb. 8 oz.	42	27	15	82	75	7
4 lb. 9 oz. to 5 lb. 8 oz.	123	109	14	44	44	..
All weights ..	220	144	76	159	132	27

conditions and admitted immediately to hospital. I do not think, however, it will ever be possible to establish these conditions but I have been helped, in forming an assessment of my results, by Dr. V. M. Crosse, of Birmingham, who has given me the results of the care of infants admitted to her premature-infant unit from home in 1944–46. The groups are very similar. I have explained that in Newcastle the special nurses tend to be called when the doctor or the midwife thinks a very small infant will have a chance of survival or when a larger infant is thought to require special attention. Dr. Crosse tells me that in Birmingham "a few infants die before admission, and naturally gross abnormalities are not admitted." Thus the groups are similar and both influenced by the same factors of selection and can be used as a basis for assessment of the home nursing. If this device is accepted as a basis of measurement, the results in the two groups can be seen to be of the same order over a birth weight of $3^1/_2$ lb. and rather less good in Newcastle below that weight. It is interesting also to compare the results from Dr. Crosse with the results of all the premature infants born and nursed at home in Newcastle during these three years (table IV). This procedure is manifestly weighting the assessment against the results of home nursing since, as I have already explained, some selection inevitably enters into those admitted to hospital. These results are given in table V and show how high a standard of care can be achieved at home under the most varied conditions.

DISCUSSION

Attempts to meet the problem of the care of premature infants born at home have hitherto been confined largely to the establishment of premature-infant units, and little attention has been given to the results of home care.

Though special accommodation is necessary for premature infants born in hospital and perhaps for a few born at home in the poorest circumstances, it is at least open to question whether it would be wise or even practical to attempt to provide hospital accommodation

TABLE IV—FATE OF PREMATURE INFANTS ADMITTED TO HOSPITAL IN BIRMINGHAM COMPARED WITH FATE OF THOSE NURSED AT HOME BY SPECIAL MIDWIFE IN NEWCASTLE

Weight	Admission to hospital from home Birmingham 1944–46			Nursed at home by special midwife Newcastle 1945–47		
	No.	Died	Survived	No.	Died	Survived
Under 2 lb. 8 oz. ..	34	30	10%	8	8	..
2 lb. 9 oz. to 3 lb. 8 oz.	117	44	63%	25	12	52%
3 lb. 9 oz. to 4 lb. 8 oz.	228	30	87%	82	7	91%
4 lb. 9 oz. to 5 lb. 8 oz.	200	11	95%	44	..	100%

for all premature infants born at home under a certain weight—e.g., 5 lb. It is particularly necessary to answer this question now that so much thought is being given to the child-health services. My opinion is that, with the expansion of the home-nursing service, improvement in training of midwives (which should be the function of a few good premature-infant units in different parts of the country), and flexible administration, the mortality of premature infants could be much reduced by home nursing; the dangers of bringing infants into hospital could thereby be avoided and, not least in these days, a more economical use made of the nursing services.

Further experience with this nursing service is obviously required both in Newcastle and in other parts of the country, and I hope that the experience of others will soon be recorded. In Newcastle we must give further consideration to the problem of the premature infant under $3^1/_2$ lb. and determine in the future whether we shall admit them to hospital or whether we can devise other methods of home nursing which will improve the results.

Finally, I wish to emphasise two important points. First, when such a service of home nursing is started, the midwives or other nurses undertaking the task

TABLE V—FATE OF PREMATURE INFANTS ADMITTED TO HOSPITAL IN BIRMINGHAM COMPARED WITH FATE OF THOSE NURSED AT HOME IN NEWCASTLE

Weight	Admission to hospital from home Birmingham 1944–46			All premature infants born and nursed at home Newcastle 1945–47		
	No.	Died	Survived	No.	Died	Survived
Under 2 lb. 8 oz. ..	34	30	10%	36	35	3%
2 lb. 9 oz. to 3 lb. 8 oz.	117	44	63%	52	32	38%
3 lb. 9 oz. to 4 lb. 8 oz.	228	30	87%	124	22	82·8%
4 lb. 9 oz. to 5 lb. 8 oz.	200	11	95%	167	14	91·6%

Digitized by Google

must actively desire to do the work and must be volunteers in the true sense of the word. They must be given a well-defined responsibility and must have the support both material and moral of administrative and pædiatric staff.

The second point of great importance is the effect of this home nursing on the family. Today, when so many of our social services and institutions undermine the confidence and strength of the family, anything in the nature of common effort which increases family ties and solidarity becomes doubly worth while.

This effect on the morale of the family was not realised when the service was started, but its significance and importance were soon apparent. The nurse in her rôle of teacher and adviser and by her personality mobilises the family for duties: someone to watch at night; someone to watch during the day; someone, probably a neighbour, to shop; everyone interested is involved and all have a sense of achievement, which gives the child a good start and is far better than if he were taken away to a hospital and returned a month or six weeks later, an unknown infant, feared and strange.

SUMMARY

In Newcastle-on-Tyne in 1945–47 the incidence of liveborn premature children was 5·7%: of 916 liveborn premature children 208 (22·8%) died in the first twenty-eight days.

Data of the results of the home nursing of premature infants are presented, and it is shown that the results for children of a birth weight above 3½ lb. are of the same order as those which were likely to be obtained in hospital.

This experiment could not have been done without the enthusiasm of the staff of the midwifery service of the Newcastle Health Department. The assessment of the results would not have been possible without the help of Dr. V. M. Crosse. To all these I wish to record my appreciation and thanks.

Births and Deaths in the Third Quarter

The Registrar-General[1] has issued the following statistics for England and Wales in the quarter ended Sept. 30 (comparable figures for the same quarter last year in parentheses):

Live births: 192,073 (216,509); rate per 1000 population 17·7 (20·0). Stillbirths: 4433 (5073); rate per 1000 live and still births 22·6 (22·9). Deaths: 101,664 (97,099); rate per 1000 population 9·4 (8·9). Deaths of infants under 1 year: 5468 (7141); rate per 1000 live births 28·0 (32·0).

The figures for stillbirths and infant mortality are lower than in any previous trimester, superseding the records set up in the June quarter this year.

Births in the U.S.A.

Changes in the circumstances attending the birth of babies are noted by the United States Public Health Service. In 1946 over 82% of live births took place in hospital; this was more than twice the percentage in 1935. Of live births outside hospital in 1946, only 5·4% were attended by a midwife or someone other than a doctor, whereas the proportion in 1935 was 12·5%. In 1946 infant mortality was 33·8, and maternal mortality 1·6, per 1000 births; the comparable figures for 1935 were 55·7 and 5·8, respectively.

Encephalitis in Japan

On July 20 an epidemic of B-encephalitis broke out in Japan, and by Sept. 11 a total of 6620 cases and 924 deaths had been reported. The outbreak, which has involved all prefectures but principally Tokyo, is now waning, according to W.H.O. figures. In the last week of August and the first two weeks of September the numbers of cases were 1389, 1081, and 585 respectively; and in the third week of September the daily total averaged less than 50.

1. The Registrar-General's Return of Births and Deaths for the Week Ended Oct. 16. H.M. Stationery Office. 6*d*.

In England Now

A Running Commentary by Peripatetic Correspondents

SINCE I read those articles on selection in the Students' Number I have felt like a layman who crawled into *Crockford* just by buying a clerical collar. Certainly I should never have been selected. After weeks of feelings of intense unworthiness I am now swinging over to mildly manic symptoms. What fools those fellows are in thinking that they can select! Do they know anything about most of the jobs for which they are selecting? About general practice? I do, I have done 250 locums, and I have never met two G.P.'s alike. Some get their results almost on personality alone, others on compassion, others—and probably the least effective—on pure erudition. Most mix all three in varying amounts. One man I knew succeeded by being a compendium of domestic and nursery medicine—*Nasturiorum folia* are "good for" lumbricus lothario, so-and-so is excellent for so-and-so. Another was a perfect genius at cross-examination, and even before the diagnosis must come the facts. There are 999 meanings behind "I have a pain in my stomach" and in twenty questions to get the right one requires genius.

Probably the one gift a G.P. must have or acquire is of being able to put himself in the patient's place—see with his eyes the sordid hopeless scene, hear with her ears the cry of the unborn, feel the longing behind the placid face, be in the factory where it happened, sense the closing walls of circumstance, glimpse the coloured toy that is the end of all desire, know the slow winding-sheet of toxæmia, the hope that flickers in old age and death, and the fear that has no feared thing. In short, sym-pathy with a hyphen, a subject not in the curriculum.

* * *

The first effect of the Act was to fill my surgeries to overflowing, rather to the justification of the cynics and the surprise of myself. But everyone had *something* wrong, and I have seen no evidence of malingering.

As time goes on one is able to analyse the manifold causes of this increase. First, many come who on getting a chill previously purchased a bottle of Dr. Quack's double-quick cure at the chemists, feeling now, not surprisingly, that if they pay insurance they're going to get value for it. (Very few of the public understand how little of the medical side of the scheme is paid from the insurance stamp.) Then of course—what we all expected and on the whole feel is a good thing—the mothers with children suffering from minor ailments and behaviour disturbances. What swells my prescription lists is for the mother to say, as she buttons up her child, "And while I'm here, doctor, I feel rather run down myself." But I think there is very little abuse. In fact, another reason for my swollen surgeries is that many come who should really be at home, forbearing to call me out; and my visiting-list is actually down a little on last year, saying much for the decency of human nature here, and I expect everywhere. When I am called out, it is with apologies, and I am touched by a small influx of little gifts in kind, meant to indicate the embarrassment of those who can't get used to not paying. The one thing that annoys me considerably is the number of patients coming for certificates for optical examination. Having no particular optical skill I cannot say that examination is unnecessary; and so I have to sign them all, an irritation both to me and the patient who has to wait. The sooner this certificate is abolished the better.

As to prescribing, I go my own way, as ever, avoiding polypharmacy as much as possible. But old dears with chronic and incurable varicose ulcers use up vast quantities of dressings and applications, and when an old boy with an asthma I am unable to cure tells me he has for years only had relief from "Inhalo," I feel justified in ordering it for him. As a nation we lean too much on a bottle of "Rep. Mist"; but it has a psychological value, and when—an earnest and unworldly beginner—I gave good advice instead of bad drugs, my patients melted away, to reappear complaining to my senior partner. So now I give a bottle of Mist.

Digitized by Google

Gent. Alk. to symbolise my presence when I'm not there.

There are two things that endanger the practice of a high standard of medicine. Firstly, a list of 4000 doesn't give one the leisure to add that bit of sympathy and wisdom that comes with spaciousness. We should be encouraged by a high capitation fee for the first thousand, and decreasing amounts for the subsequent ones. Secondly, the minor specialties. During the war I became a graded psychiatrist, and learned a lot. But if I wish to give psychiatric treatment to patients on my list, and this implies hours of patient endeavour, I must do it for seventeen bob a year, or love. Likewise circumcisions. My patients like them done when the baby is a week old and the nurse still in attendance; they don't like going to hospital. Well, I do *some* for the love of it, but I'm only human, and the hospital lists will soon be more swollen than ever. (Jolly good job, you may say; G.P.'s should know their place and not try to be specialists.)

If you ask whether the doctor-patient relationship has been altered I say emphatically "No." Good or bad, it's the same as before and depends on the personalities of both.

P.S.—An irritating side issue. Why are patients told that the chemist will provide a bottle for every prescription? Doesn't this encourage waste and thriftlessness?

* * *

These hospitable columns record from time to time the experiences of the vast band of brothers seeking appointments. Lately we were given some advice on how to supply a photograph, and the reluctant conclusion was drawn that it was better to stick to a misty representation of one's own dial than to risk all on a photo of James Mason or Greer Garson. Now a new phenomenon has come to my notice—the psychological interview.

It appears that the psychologists, still flushed with triumph after selecting many thousands of Army officers (and they did very well, for all the officers I met, however young, could read and write and some of them had charming manners), are not content with organising house parties for the Civil Service, but are lending their skill to medical selection boards. The technique of the interview is strange. No waiting about in draughty corridors suspiciously eyeing other candidates, but formal introductions all round, free cigarettes, and reassuring talk about expenses from charming secretaries. The half dozen candidates and the selection board then settle themselves round a long table for several hours' discussion. Tea arrives and more cigarettes. By this time all suspicion is lulled and there is a friendly atmosphere comparable to that in a railway compartment where the train is not more than two or three hours late and no actual discomfort has yet been suffered.

At this point the candidate must exercise extreme vigilance, for now the psychologist will tenderly inquire whether those concerned approve of this method of selection. On no account say that you cannot see any point in the whole performance and would like to know the criteria of the selection committee. Comments of this sort merely reveal to the committee unpleasant traits of obstructionism and negativism which it is your duty, as a humble person merely seeking to earn your bread and butter, to conceal. Rather, confine your remarks to vaguely phrased but enthusiastic murmurs of appreciation.

On the whole I prefer the old-fashioned board, largely composed of unknown but obviously eminent lights of the profession, who treat one with grave courtesy for twenty minutes and then appoint the chap who has already held the job for two years.

* * *

In America there is everything in the shops which we used to have before the war, plus all that has been created by advancing technology. Perhaps one might advance the thesis, though, that the principal function of the man (and even more the woman) in the street, is that of consumer; an indispensable necessity to the manufacturer, for whom the world was created. At home, of course, there still lingers the notion that the world was created for the man in the street.

Letters to the Editor

INFANTILE GASTRO-ENTERITIS AND STREPTOMYCIN

SIR,—I have read with great interest the paper by Dr. James and her colleagues (Oct. 9) and last week's letter by Dr. Anderson and others.

During the 1947 epidemic of infantile gastro-enteritis at Aberdeen, which involved 207 cases with a fatality-rate of 50·6%, an extensive study of the ætiology of this condition was carried out, the first results of which were published earlier this year.[1] Two serologically distinct types of *Bacterium coli* were isolated in close association with the disease, and one of them was identical with an organism described by Bray [2] in connexion with similar cases. This particular type was recovered in 94·7% of cases, and in only 1·8% of 721 controls. Both organisms were found to be highly susceptible to streptomycin in vitro, being inhibited by 0·4–0·8 μg. per ml.

Later in the year Dr. C. Gibson, of the Presbyterian Hospital in New York, sent a small quantity of streptomycin which enabled us to commence clinical trials with this antibiotic. Owing to the small number of cases so far treated, results are as yet inconclusive, but rapid clinical improvement took place more often in treated than in untreated cases in the same epidemic; and this clinical improvement coincided with the complete disappearance from the stools of the coliform strains in question. As Dr. Anderson and others have already stressed, nearly all gram-negative organisms tend to disappear from the fæces when streptomycin is exhibited by mouth, and to a lesser extent when it is given parenterally. It is true that *Bact. coli* as well as *Proteus* and paracolon bacilli reappear soon after cessation of streptomycin treatment, but in our own cases the suspected types of *Bact. coli* did not recur and recovery was uninterrupted.

During the first half of this year, at Stoke-on-Trent, I isolated the same organisms in 25 out of 32 cases of gastro-enteritis, most of which were fatal. Only 2 were treated with streptomycin; both patients were extremely ill on admission, both improved dramatically on streptomycin therapy, and in both the coliforms in question disappeared and did not recur.

I should most warmly welcome the release of streptomycin for the purposes of investigating this form of treatment.

Pathology Department, Stoke City General Hospital. C. GILES.

RECURRENT DISLOCATION OF THE SHOULDER

SIR,—Evidently Mr. Richardson is unfamiliar with my operation for recurrent dislocation of the shoulder, for in his article of Oct. 16 he has got it wrong in almost every detail and he has created a number of difficulties which in fact do not exist.

The cause of recurrent dislocation is avulsion of the capsule with or without the glenoid ligament from the anterior margin of the glenoid cavity, and the only rational treatment is to reattach the capsule to the bone from which it has been torn. Most of the cases occur in powerful athletic young men who have anything but weak muscles. I agree that bone lesions, when present, are the result and not the cause of the dislocation. They do not affect the treatment or the prognosis. Mr. Richardson says:

1. "An attempt is made to repair the capsule." This is incorrect. The capsule is divided over the glenoid margin and its cut edge is fixed to the bone which has been freshened to receive it.

2. "The lesion is situated deep down in a narrow wound which easily fills with blood." Inadequate exposure and imperfect hæmostasis are, next to sepsis, the commonest causes of bad surgical results. In my operation the lesion is completely exposed and readily accessible, and every bleeding-point can be seen and controlled. It is not true that a

1. Giles, C., Sangster, G. *J. Hyg., Camb.* 1948, **46**, 1.
2. Bray, J. *J. Path. Bact.* 1945, **57**, 239.

Digitized by Google

haemarthrosis is likely after any procedure which involves opening the shoulder-joint.

3. "The difficulties in drilling the necessary holes in the glenoid cavity and in inserting the sutures are great." Since I introduced the dental drill for this purpose, some ten years ago, these difficulties have been completely overcome. My only regret is that I did not discover the drill until my second paper (1938) was in print.

4. "Even if the torn structures are reapposed, there is considerable doubt whether they will be permanently united by the formation of fibrous tissue." There is no doubt whatever. When properly done, the fixation of fibrous tissue (capsule, ligaments, or tendons) to bone is as certain as anything in surgery.

5. "During the spasms which occur when the patient is coming round from the anæsthetic. . . ." Our patients do not have postoperative convulsions or spasms, and the suggestion that it is impossible to suture a muscle (subscapularis) securely, because the stitches will be torn out by muscular spasms, is most extraordinary.

6. "The coracobrachialis muscle and the short head of the biceps muscle . . . by their contraction will tend to pull this fragment (of coracoid process) downwards; . . ." But surely Mr. Richardson is capable of fixing this piece of bone in place so that it will not be pulled down. Elongation of the coracoid process is no part of my operation.

We have a safe and certain cure for recurrent dislocation of the shoulder. It is a straightforward repair of a definite and constant lesion. It does the least possible damage to the surrounding parts and it practically restores the joint to its normal condition. It is not difficult and it is within the competence of any surgeon of ordinary ability. It seems unnecessary to add yet another bone-block operation to the list of irrational procedures which ignore the true pathology of this condition and attempt to cure the dislocation by roundabout means.

London, W.1. A. S. BLUNDELL BANKART.

BEDS FOR PULMONARY TUBERCULOSIS

SIR,—Perhaps you will allow me to reply to Dr. Houghton's comments in your issue of Sept. 4. I cannot accept his suggestion that shortage of beds leads to confusion of motives in selecting patients for admission. Surely, under such circumstances the case which has the greatest claim for admission is the one which appears to be most likely to benefit by the available treatment. If the resources comprise only a nursing staff, then perhaps the accommodation should be used to help the chronic invalid. If, on the other hand, the facilities are those of a great modern thoracic hospital, surely the patient admitted should be one able to benefit most from such amenities. The question of an individual or social problem should not complicate the issue.

Now, I certainly have a bias toward collapse therapy for suitable cases of pulmonary tuberculosis, but I do not believe in the "crash A.P.," or that quick collapse should be the sole worthy objective in treating phthisis; but equally, I should not like to feel it on my conscience that a patient's health had been jeopardised by my unwillingness to induce a pneumoperitoneum or pneumothorax. Few will dispute that the prognosis of the B2 or B3 case of tuberculosis, conservatively treated, is bad—half the cases will be dead in two years. There is increasing evidence that efficient collapse measures can substantially improve the outlook, and the best yardstick by which to estimate initial efficacy is sputum conversion.

If one aims at a programme of collapse measures for as high a proportion of cases as possible, they must be diagnosed and dealt with early; a delay of nine months before admission is a substantial slice in the average consumptive's remaining expectation of life. In this town it may be that phthisis is diagnosed early: at any rate there are less than 2000 people to each general practitioner, and over 2300 new patients were referred to me in 1947, yielding 95 (4%) sputum-positive cases.

I feel confident that if Dr. Houghton's suggestions for supplementing nursing staff and absorbing waiting-lists can be realised, the results of collapse treatment generally will be greatly improved.

Tuberculosis Dispensary, Reading. W. H. TATTERSALL
Chest Physician.

UNFORTUNATE NAMES OF HOSPITALS

SIR,—I hope that you will strongly support the suggestion by "A.B." in his letter of Oct. 16.

It was perhaps to be expected that the desirability of improvement should have occurred first to psychiatrists, but the general use today of the term "mental hospital" where other more frightening titles were in use only a few years back, shows that it is possible to make such changes. If it be objected that moneys are given or bequeathed and could not be claimed if the name were changed, I would suggest that there are ways round such a difficulty; even a private Act of Parliament should surely be possible to achieve a worth-while object like this.

That this suggestion by "A.B." is likely to appeal to you, Sir, is evident from the annotation on the Patients' Hospital in your issue of Feb. 21. Now that the need for the change has been pointed out, all those in a position to act will be glad to contribute to lightening the burden on patients and relatives of patients with "cancer," "consumption," and "incurable" maladies—a burden which it is not easy for doctors to appreciate.

Guy's Hospital, London, S.E.1. RONALD MAC KEITH.

HYALURONIDASE AND GONORRHŒAL INFECTION

SIR,—In 1929 Duran-Reynals[1] reported that the intradermal injection of testicular extract caused rapid dispersal of fluid, toxins, and particulate matter from the point of injection into the surrounding skin, and that extracts of other tissues had no such effect. This result, he suggested, was due to a change in the cells of the host brought about by some substance present in testicular extract which he termed the spreading factor. Later McClean[2] confirmed these results, and finally Chain and Duthie[3] produced evidence that the spreading factor was hyaluronidase, an enzyme which acts specifically on its substrate hyaluronic acid, which is present only in the skin, vitreous humour, and synovial fluid but absent from all other body tissues. Chain and Duthie, among others, also found that some bacterial cultures produced hyaluronidase, but they disagreed with the report of Meyer et al.[4] that hyaluronidase was present in extracts of some other tissues—e.g., ciliary body. They concluded that hyaluronidase in the body was present only in testicular extract and that, bacterial contamination was responsible for the findings of Meyer et al. Finally Robertson et al.,[5] investigating cultures of various pathogens, reported that the gonococcus could not produce this enzyme.

The fact that the tissues associated with the enzyme and its substrate are the genital tract, eye, joints, and skin, which are also those affected in gonorrhœal infection, makes it difficult to believe that this association can be fortuitous. Further, the mode of invasion, the direction of spread, and the complications of gonorrhœal infection show that hyaluronidase may well play a very important part in this disease.

Invasion of the male anterior urethra by gonococci from the urethral orifice and their later extension to the posterior urethra, prostate, seminal vesicles, and epididymides is difficult to understand because (1) the gonococcus is non-motile; (2) the anterior urethra for some distance from its orifice is covered with a naturally resistant flattened epithelium, and a further barrier to proximal extension is found in the relatively resistant membranous portion; and (3) the natural direction of flow in the affected parts is distally. I suggest that the hyaluronidase in the spermatic fluid lining the urethra after coitus acts as a chemotaxic agent facilitating the spread of the infecting organisms to the non-resistant epithelium of the anterior urethra, which they penetrate, giving rise later to acute gonorrhœa. That hyaluronidase may act in this way is shown by the fact that, if two

1. Duran-Reynals, F. *J. exp. Med.* 1929, **50**, 327.
2. McClean, D. *J. Path. Bact.* 1930, **33**, 1045; *Ibid*, 1931, **34**, 459.
3. Chain, E., Duthie, E. S. *Nature, Lond.* 1939, **144**, 977; *Brit. J. exp. Path.* 1940, **21**, 324.
4. Meyer, K., Hobby, G. L., Chaffee, E., Dawson, M. H. *J. exp. Med.* 1940, **71**, 137.
5. Robertson, W. V., Ropes, M. W., Bauer, W. *J. Biol. Chem.* 1940, **133**, 261.

Digitized by Google

culture tubes, one containing hyaluronidase and the other not, are placed in a medium containing organisms, the organisms tend to accumulate about the mouth of, and invade, the tube containing hyaluronidase. With the onset of acute urethritis favourable conditions exist for the infection to overcome the barrier presented by the membranous portion of the urethra, since priapism and its accompanying automatic secretion of spermatic fluid are common features of this stage of gonorrhœa. Direct spread to prostate and vesicles follows naturally, and extension to the epididymides is more satisfactorily explained on this hypothesis than by either the accidental entrance of infected urine via the vas deferens or by lymphatic spread.

The complications of gonorrhœa—iritis, rheumatism, and keratodermia—are always associated with extension of the gonococcal infection to prostate, vesicles, an epididymides, where drainage is poor owing to anatomical structure. Therefore it seems reasonable to suggest that, owing to poor drainage, hyaluronidase and organisms are absorbed into the blood-stream, act on the susceptible tissues (containing the substrate hyaluronic acid), and so bring about the known pathological changes.

Apart from gonorrhœa, there may be a wider pathological significance in hyaluronidase and its substrate, since clinical experience shows that the removal of septic foci is followed by cure in some cases of rheumatism. It would be of interest to know if the infecting organisms in these cases could produce hyaluronidase, since Robertson et al.[5] showed that some strains of pathogens—e.g., streptococci and *Cl. welchii*—produced hyaluronidase in culture, and they suggested that it might play a part in rheumatoid arthritis. The latter possibility will, I feel sure, be found to be incorrect; on the other hand, the isolation of a group within the rheumatic diseases may be shown to depend on a hyaluronidase-producing organism from a septic focus. The fact that bee venom is a traditional therapeutic agent in the treatment of rheumatism and contains hyaluronidase suggests that the results of this treatment are possibly due to the formation of an anti-hyaluronidase.

London, W.1. F. L. LYDON.

DENTURES AND ANÆSTHESIA

SIR,—As one who has been engaged in making artificial dentures for thirty-six years, and who has been interested and engaged in administering anæsthetics for dental operations, I would like to enter an emphatic protest against Dr. Parry-Price's [1] practice of leaving dentures in place during anæsthesia. Any dentist or dental mechanic of experience will agree that no denture material yet made can be guaranteed against chipping. There is surely enough risk of portions of natural teeth and fillings becoming detached, without adding to the danger with pieces of porcelain or acrylic resin (the latter, by the way, being opaque to X ray).

For some time I have noticed that either face-piece or nose-piece obstructs the breathing by its very pressure on the levator nasi muscle—an observation confirmed by anæsthetists to whom I have spoken. Consequently, I am endeavouring to devise an inhaler in the form of a metal or plastic box which would rest upon the forehead, its top end plugging directly into the large-bore tube of the anæsthetic apparatus, and having at its lower end two soft metal tubes, bent so as to enter the nostrils, each fitted with a soft rubber "stall" to ensure an air-tight fit and prevent damage. Such an inhaler would, I think, not only overcome the stifling feeling that our patients complain of, but always maintain a good airway, no matter how hollow the patient's cheeks.

Lyme Regis. ERNEST H. PHILLIPS.

SIR,—Every anæsthetist must sympathise with Dr. Parry-Price in the difficulties he mentioned in his letter last week, and he is to be congratulated on his experience of leaving full dentures in position during anæsthesia. Unfortunately not every anæsthetist is careful, and all are human, and I cannot help feeling that it is better that nurses should still be taught that all dentures should be removed before operation, than that the occasional single tooth should slip into the trachea; certainly an exception might be made in the case of the patient who strongly objects on cosmetic grounds. Dr. G. J. Rees and I described in THE LANCET (Feb. 21) a buccal support for the edentulous which we felt was as adequate as, and yet safer than, a full denture.

I confess that I have more confidence in passing a laryngoscope in an edentulous patient than in the presence of a full set of teeth.

St. George's Hospital, London, S.W.1. D. D. C. HOWAT
Anæsthetics First Assistant.

1. *Lancet*, Oct. 23, p. 670.

CAROTID-SINUS SYNDROME

SIR,—From the point of view of clinical diagnosis the case described last week by Dr. Turner and Professor Learmonth is interesting. They certainly proved that this man had a hypersensitive carotid-sinus reflex, but I am not so sure that his attacks of intense vertigo, staggering, and vomiting were due to this. These are not the symptoms usually produced by cardiac asystole, and this man's spontaneous attacks never seem to have followed the usual pattern of syncope or convulsions. In my experience it is very difficult to assert that a labyrinthine cause of vertigo is excluded: tinnitus and deafness may not occur till much later, and I doubt if tests are decisive. Remissions of labyrinthine vertigo may last for months or years.

I venture to think that the diagnosis in this case remains in some doubt.

Newcastle-on-Tyne. F. J. NATTRASS.

DEEPER AND DEEPER

SIR,—In your issue of Sept. 4 (p. 399) I read with interest that a British diver, Petty Officer Bollard, reached a depth of 535 ft. in Loch Fyne on Aug. 28, thereby beating the former record for deep diving set up in 1945 by the young Swedish engineer and diver, Arne Zetterström. Mr. Bollard and the Royal Navy, which has always contributed in such a splendid way to the development of diving, are to be congratulated on a new and extremely good achievement.

I am, however, anxious to make some comments and corrections to your note. When the dive during which Zetterström died was made on Aug. 7, 1945, the depth reached was not 480 ft. but 525 ft. (160 metres). Zetterström made this descent, as he had so often before, using a synthetic gas mixture (hydrogen with 4% oxygen) of his own invention. He died on his way to the surface. It should, however, be emphasised that his death was not due to any inherent deficiency in the method. He attained the great depth aimed at without difficulty, and at that time this depth, of 160 metres, was the world record for open-sea diving in a flexible diving-suit. The ascent also proceeded quite normally at first. Owing to a grave mistake on board the diver's boat, a wire (guy) attached to the diving platform was brought home too rapidly and not in accordance with the previously calculated decompression tables. From a depth of approximately 164 ft. (50 metres) the diver was thus suddenly brought directly to the surface. Zetterström died from acute lack of oxygen and violent decompression sickness.

Two articles have lately been published on the Zetterström method for deep diving with hydrogen. One of these is a translation of a paper written in 1945 by Zetterström himself [1]; in the other Bjurstedt and Severin [2] discuss the physiological aspects of the method.

As far as I am aware, 535 ft. is still the world record for open-sea deep diving. However, it may be pointed out that Behnke, in a report (1947) from the U.S. Naval Medical Research Institute, Bethesda, entitled "A review of physiologic and clinical data pertaining to decompression sickness," mentions a simulated dive to a depth of 550 ft. in a wet pressure tank in April, 1945. A helium-oxygen mixture was breathed and the diver remained in good condition throughout the period of the dive and afterwards.

Your short notice does not mention the kind of gas mixture breathed by Mr. Bollard. In view, however, of the narcotic effect of nitrogen and the great breathing

1. *Milit. Surg.* 1948, **103**, 104.
2. Bjurstedt, H., Severin, E. *Ibid*, p. 107.

Digitized by Google

resistance, it does not seem probable that the gas breathed was ordinary air. Further information on this point would be very welcome.

Office of the Surgeon-General, Royal Swedish Navy, Stockholm. GUSTAF SEVERIN.

DOSAGE OF SULPHETRONE FOR CHILDREN

SIR,—In 'Sulphetrone' treatment a blood-level of between 7 and 10 mg. per 100 ml. would seem to be desirable. The dose recommended for children under 4 years of age given in published papers [1] and by the manufacturers is 0·5 g. daily for the first week and 1 g. daily for the second week.

Of two children under 4 years of age treated with sulphetrone in this hospital, one, aged 2 years, weighed 13·2 kg., and the other aged 3 years, weighed 11·5 kg. In these children the dosage was gradually increased until a blood-level of 7–10 mg. per 100 ml. was obtained. The first child required 6 g. and the second 3 g. of the drug daily. This dose would correspond to a dose of about 24 g. and 16 g. per day in an average adult.

Thus it would seem necessary to step up the dosage of sulphetrone in young children, in the light of blood estimations, as the optimum dose may be relatively high.

Department of Pathology, Children's Hospital, Sheffield. J. L. EMERY.

PRODUCTION OF INSULIN

SIR,—The four British manufacturers of insulin—namely, Allen & Hanburys, Boots Pure Drug Co., British Drug Houses, and Burroughs, Wellcome & Co.—are a little concerned lest the annotation in your issue of Oct. 9 might lead to certain misleading conclusions. I should like to quote from a letter by me in the *Times* of July 23.

"... I would like to comment on the article from your Medical Correspondent entitled 'Need For More Insulin' which appeared in your issue of July 16 and which referred to the report on insulin in the April issue of the *Chronicle of the World Health Organization*. Production of insulin in this country is adequate to meet in full both home and export demands, and ample stocks are always maintained in this country. The implication in the report that the United States has only a small exportable surplus is surprising, as British manufacturers are meeting active American competition in most of the important markets of the world and are having to fight hard to maintain their own exports of insulin. Great advances have been made in the yield of insulin from pancreas as a result of the collaboration of our research teams, and there will be no relaxation of our combined efforts to achieve even better yields. The methods of collection of pancreas stated to have been recently discovered in Germany have in fact been widely known for some time; they are at best a makeshift. Immediate refrigeration of pancreas glands on removal from the animal is still a necessity if the best yields of insulin are to be obtained, and it is important that no one should get the impression that pancreas should be collected in this country other than under ideal conditions. Finally, we would emphasize that our production facilities alone could provide at least double the present quantity of insulin produced if the demand for it should arise."

There is every reason to suppose that the methods of collection being used in Germany are merely designed to ensure that pancreas is not totally wasted in slaughter-houses where adequate refrigeration facilities are not available.

Ware, Herts. JOHN C. HANBURY, Chairman, British Insulin Manufacturers.

PSYCHOGENIC RHEUMATISM

SIR,—I regret that I did not have an opportunity of hearing Dr. Philip Hench's lecture on psychogenic rheumatism, annotated in your columns on Oct. 23. It would be interesting, however, to learn how many of the large number of clinicians who too commonly diagnose psychogenic rheumatism have ever taken the trouble to dissect out the spinal joints post mortem. They must be extremely few. Meanwhile, the post-mortem appearances of hysteria remain protean.

London, N.4. I. H. MILNER.

1. Madigan, D. G. *Lancet*, July 31, p. 174.

PROPRIETARY MEDICINES UNDER THE NATIONAL HEALTH SERVICE ACT

SIR,—I am afraid Mr. Godding's reply to my letter rather obscures the issue. He has given the usual accepted definition of "ethical," but has failed to point out that there are many borderline cases. In giving the doctor carte-blanche to order proprietaries, provided he can justify the prescribing, the authorities have avoided this difficulty and shown their confidence in the doctors. Mr. Godding's article did not state that the proprietary articles ordered on N.H.I. and private prescriptions were all of the truly ethical type. The comparison N.H.I./private is now of course invalid, since the two are merged, and data collected by the *Chemist & Druggist* after July 5 over the whole country suggested that doctors were not wholly ignorant of their right to prescribe proprietary articles.

I suggest, Sir, that a lot of the research ascribed to proprietary articles is attributable to ethical proprietaries of the truest form, which we are agreed receive proper support; and that to introduce other proprietary articles needs—apart from normal business financing—no special research. No doubt there are some pages of the book left closed when claims of this sort are made. How many different compounds of aspirin and codeine are on the market under different trade names?

It is up to the authorities, when reviewing the cost of the N.H.S., to decide what future policy to adopt; and it is clear that the trade interests will make their views felt. But if Mr. Godding and other manufacturers were to stimulate, by intensive advertising, the prescribing of proprietary medicines at present they would probably prejudice their own future. Prescribing such as that cited by Mr. H. Davis, D.SC., at the National Association of Women Pharmacists' meeting on Sept. 22 is bound to have unfortunate results.

I still feel that the Chemists Federation cannot properly undertake the therapeutic assessment of proprietary medicines. In order to improve its own standing, I think the C.F. would be well-advised to drop price protection, and leave that to the Proprietary Articles Trade Association. This would at any rate mean that items on the C.F. list were accepted on merit. Also it would mean, in my view, that the C.F. would be more seriously considered by some of the eminent pharmaceutical manufacturers who do not wish to be included in the list at present.

With careful reading of my contributions to this question, I think Mr. Godding will agree that there is no real fundamental divergence of views. I shall be happy to place before him in confidence those of the C.F. articles which are, in my view, undesirable.

In closing may I say that I have just seen a publication "Bayer Products/N.H.S." May I congratulate this firm on having sufficient confidence to give this information in the form stated.

Seaham. A. FORSTER.

COMPULSORY ADMISSION

SIR,—X.Y.'s letter of Oct. 23 is opportune. In London, the problem of gaining admission to hospital for the elderly patient exists with regard to acute as well as chronic illness. It is well known that the Emergency Bed Service often has great difficulty in finding a bed for a patient over 70, even when the only doctor who has examined him has certified that he requires urgent admission. Some hospitals are more coöperative than others, so the burden of these patients is apt to fall on the "willing horse": for example, a hospital has recently admitted, from as far as twenty miles away, a man of 72 with a strangulated hernia, a woman of 81 in coma, and a case of abortion. In each case the E.B.S. had been refused admission for these patients by 15–20 other hospitals situated nearer to the patients' homes.

Unless hospital medical staffs become more coöperative, so as to solve this problem rapidly for themselves, it will obviously be necessary for a higher authority to give a definite directive allocating the responsibility for all unwanted patients in a specified area to individual hospitals or hospital groups.

London, N.19. T. ST. M. NORRIS.

Digitized by Google

CONVALESCENCE: FEE OR FREE?

SIR,—Since July 5 the arrangements for providing children with convalescent treatment have been changed; as the new machinery comes into use, certain defects have appeared. Before that date convalescent treatment for school-children (at least in London) was largely provided through the Invalid Children's Aid Association, though much of the actual cost was defrayed by local education authorities. The system worked reasonably well. The association accumulated a good deal of information about the convalescent homes, which enabled them to place the children in the appropriate ones, and the education authorities accepted their responsibility to pay. It was with the laudable intention of removing this burden from the rates to the national exchequer that the new procedure was set up in the National Health Service Act.

The Ministry of Health has classified the former convalescent homes into two groups: (1) "holiday homes," where medical and nursing treatment is not provided, and (2) "convalescent homes," where such treatment is provided. The second group has been taken over by the regional boards, but the first group has not. So treatment in a convalescent home is free; but when given in a holiday home somebody has to pay the bill—the parents if they can afford it, or else the education authority or a charitable fund. This puts a school medical officer in a difficult position when he has to decide which type of home to recommend for a convalescent child—either a convalescent home, maintained by national funds, or a holiday home, when his own authority may be asked to foot the bill. His inclination to plump for the former will be reinforced by two powerful arguments. First, some authorities, thinking that all convalescent treatment would be free, have made no financial provision for it after the appointed day; and secondly, it is hard to see what sort of convalescent can do without medical and nursing treatment. The sequel might have been foreseen: convalescent homes have long waiting-lists, holiday homes stand empty; and the children suffer.

Other anomalies have arisen. Some holiday homes do provide treatment for some of their patients—e.g., they may have a ward reserved for heart disease. A child sent here will have to be paid for, though exactly the same treatment in a neighbouring institution would be free. Accommodation for this type of patient is scarce, so these wards should not be closed. It is not yet clear whether regional boards will arrange all convalescent treatment centrally, or will leave hospital and local-authority welfare services to find accommodation directly with the homes. In either case, the valuable knowledge garnered by the I.C.A.A. through years of experience is likely to be lost.

I appreciate that these difficulties are the teething troubles of the new scheme, and I point them out in the belief that it is best to do so early while procedure is still fluid.

Whipps Cross Hospital, London, E.11. E. HINDEN.

*** As we remarked in an annotation on July 24 (p. 153), it is clearly contrary to the principles of the Act that some patients should have to pay for a period of recuperation in a home when others do not; and it seems an unnecessary complication that the cost of holiday homes should fall on local authorities while that of convalescent homes is met by the regional boards. Our suggestion that other hospitals should follow the lead of some teaching ones in paying the holiday-home fees for their own convalescents would still leave a large class of convalescent children unprovided for.—ED. L.

LETTER TO A NEPHEW

SIR,—The final paragraph in the original letter (pre-Nelson) proves the author so sensible of true values that it should dismiss X.Y.Z.'s fears. These arose from a few earlier phrases, directed, I think, against "narrow-minded fanaticism," rather than the following of the vocation of healing—a very practical idealism, involving a deliberate devotion to the relief and encouragement of fellow men and women in distress. Our profession, most of all that of a general practitioner, gives supreme opportunities of generous response to human need and suffering. Yet the patient needs something more than his doctor's devotion: he needs his wisdom, his skill, and his character of truth and honour. These are fruits of toil and resolution. Thomas à Kempis says truly: "He doeth much that loveth much," but immediately adds: "He doeth much, that doeth a thing well."

G. R. G.

Obituary

PERCIVAL PASLEY COLE

O.B.E., M.B. BIRM., F.R.C.S., L.D.S.

Mr. P. P. Cole, whose death on Oct. 19 we announced last week, made his mark as a surgeon of wide interests who contributed particularly to plastic surgery and the surgery of hernia. Much of his professional life was devoted to the welfare of seamen, and two years ago he was elected an honorary member of the National Union of Seamen.

Born seventy years ago at Weymouth, he received his early education at Weymouth College, from which he went on to Guy's Hospital. He qualified as a dental surgeon in 1899, and five years later took the Conjoint qualification. After house-appointments at his parent hospital he passed the examination to become, in 1906, F.R.C.S. Three years later he graduated as M.B. at Birmingham, where he had gone as lecturer in anatomy. He returned to London in 1910 as demonstrator of anatomy at the Middlesex Hospital; and in the two years which followed he was appointed surgeon to Queen Mary's Hospital for the East End, surgical registrar at the Royal Cancer Hospital, and assistant surgeon to the Dreadnought Hospital. The association with these three hospitals continued throughout his life.

Elliott & Fry

During the first world war Cole turned his dental training to good account in the treatment of maxillo-facial injuries at King George's Hospital, Waterloo Road; he also served as surgeon at the Brook War Hospital. In 1919 he succeeded C. C. Choyce as dean of the London School of Clinical Medicine, which had been established at Greenwich in 1910. Here he gave special thought to the postgraduate training of ship's surgeons, providing for them opportunities to reside in hospital during their periods of leave. Latterly he took an important part in the revision of the *Ship Captain's Medical Guide*, originally composed seventy years ago by the medical superintendent of the Dreadnought Hospital Ship—the forerunner of the shore hospital.

A. D. recalls that, in order to gain closer knowledge of seamen's needs, Cole himself went to sea as a ship's surgeon. "Out of this knowledge and experience he strove constantly to enhance the status and prestige of ship's surgeons, in association with Gwynne Maitland and other medical superintendents of the shipping companies." He also campaigned for the establishment of a diploma for ship's surgeons; but this scheme, when well advanced, was interrupted by the second world war. During the war his retirement from the Royal Cancer Hospital was deferred; he continued as surgeon and venereologist at the Seamen's Hospital; and he gave valuable assistance as superintendent in the E.M.S. In 1946 he retired from the active staff of the Royal Cancer Hospital, and in 1947 from the Dreadnought Hospital. In 1947 he was appointed O.B.E., and this year he was elected a vice-president of the Seamen's Hospital Society.

"Cole's interest in surgery was broad," writes A. H. H., "but there were two main channels into which his activities became directed—the filigree operation for inguinal herniæ and plastic surgery. The former was an inheritance from McGavin at the Seamen's Hospital,

Digitized by Google

but it was Cole's dexterity which perfected the operation, and his lucid writings on the subject which brought it to the attention of surgeons and kept it in focus during a phase of surgical development in which the use of non-absorbable suture material was at a discount. His valuable work on plastic surgery is recorded in various articles on war wounds and injuries, the reparative surgery of the upper limb, and the surgery of the jaw and face. He blended this knowledge and skill in plastic surgery with an intimate understanding of the pathology and treatment of malignant disease. 'Cancer is indivisible,' was a favourite dictum, and he was a persistent advocate of team-work. His opinion, planned treatment, and operative skill in cancer of the face, scalp, and mouth was of great value in an institution such as the Royal Cancer Hospital where he continued with this work up to a short time before his death. His last contribution to the literature, published three months ago, concerned such a case. At the age of 70 he still possessed an active mind filled with original ideas based on sound and logical principles.

"His forthright statements and unwavering principles caused him to be respected by all who worked with him. This fearless, honest, and single-minded approach to all difficulties sometimes made his passage through life turbulent, but his sense of justice and tolerance won for him a lasting admiration and affection."

He is survived by the son and daughter of his first marriage, and by his second wife, Dr. M. P. C. Greene. A memorial service is to be held at the Royal Cancer Hospital this Saturday, Oct. 30, at 11 A.M.

HENRY SMITH

C.I.E., M.D. R.U.I.

IN the early years of this century many ophthalmologists visited India to study Henry Smith's work at his hospital at Jullundur on the surgery of cataract extraction, and in his monograph published in India in 1910 Lieut.-Colonel Smith described his operation for intracapsular extraction of the crystalline lens. After his retirement he published a revised edition in 1928 which set out the improvements he had devised on this original technique.

Colonel Smith was born in Clogher, co. Tyrone, in 1862, and was educated at Queen's College, Galway, and the Royal University of Ireland, where he graduated in medicine in 1888. Two years later he joined the Indian Medical Service, and he served in the Punjab until his retirement.

In the 1914–18 war he was appointed consulting ophthalmologist in Mesopotamia, and in 1921 he returned to England and settled in Sidcup, where he continued to write and practise. Accompanied by his son, Dr. Joseph Smith, he revisited India and later Dr. Barraquer in Spain. After his tour of the United States, where he won honour, affection, and many followers, he re-edited his book on cataract. With the graphic illustrations by Dr. Derrick Vail, and mathematical considerations by his son, it has become a classic. The ill health of his wife and of his son, and their need of continuous care which he undertook, led him to return to his birthplace in Northern Ireland, where he died, on Feb. 29, in his 86th year.

One of his American friends writes: "Colonel Smith stood six foot four, mentally, physically, and morally. Big, handsome, and impressive, he possessed a wise sense of humour, a combative versatility, and a pair of hands that were well-nigh perfect surgical instruments. As a practical anatomist he was convincingly logical, and his sensitiveness to tissue response was uncanny. These characteristics led him to find in his general surgery the conclusive argument for intracapsular rather than extracapsular extraction of the lens, and, with the utilisation of enormous material, to conquer both difficulty and opposition. He maintained that accidental and traumatic expulsion of the lens in capsule had, willy-nilly, demonstrated that here as elsewhere, complete removal of diseased or useless tissue, where possible, is correct surgery. He sought and perfected a definite technique, and dismissed the objections of difficulty and danger as fear and insufficient skill which time and practice would banish. . . . His lifelong battle began on the plains of India. This appreciation is born in the new world. East and West pay tribute."

Colonel Smith married Miss H. D. Russell and they had two sons.

THE LATE DR. WESTERN

G. T. Western (known as "Daddy" or "Father" by his friends of both sexes) was a remarkable character. At the London Hospital this was known only to his intimate friends; the life of a bacteriologist at the medical school of a big teaching hospital is apt to be rather impersonal. But all his splendid qualities came into play at St. Hugh's, the Military Hospital for Head Injuries, to which he came from retirement in 1940 as a lieutenant aged 63. He became an institution, a man of whom many stories are still told by men who were at St. Hugh's. Everything that he undertook was done with an unusual degree of competence. Although much of his life was spent in London he was a man of the country, a craftsman steeped in country lore, which he had matched with his practical knowledge of science and his sense of business. He understood the ways of bees, how to keep oatmeal, where to buy the best saws, how to fell trees, how to store apples, how to keep the badgers from his hens, how to draw blood from the smallest veins, and so on. His standards never deviated.

At St. Hugh's he ran his laboratory easily, conserving its staff from threats of posting with a morose and almost savage effectiveness. He found time for many other things: he ran the Officers' Mess with supreme efficiency, grew vegetables on its lawn, chopped its wood, and tended bees for the Mess and for various Oxford matrons. At this stage of his life, though he was still a highly competent bacteriologist, bees interested him more than bacteria. He did the Mess shopping in a way that gained the respect if not the approval of Oxford tradesmen. Said one lady to a local shopkeeper, "Do you know Major Western, the bee expert?" "B— expert," said the shopkeeper ruefully, "Yes, that's just about what he is!" He established a record for low cost-of-living in Officers' Messes and imposed his rigorous way of life—open windows, meagre fires, no black market, no second helpings—with unbending firmness upon a highly individualistic group of neurologists. To everyone he was at times intimidating, with a short and very direct comment followed by a prolonged and penetrating, reproachful stare over the top of his spectacles. Severe reprimands to all, regardless of rank, endeared him to junior officers. All knew that his bark was worse than his bite, that he was the kindest, fairest, most unselfish, and most generous of men, ungrudging in his service to them and to the hospital. This spartan life was part of his war against Hitler. He was an unbreakable rock, as could be felt by all in the bad days of 1940, and again when he had news that his son's cruiser had been sunk, followed, after a weekend of darkness, by a cable that all was well. By his qualities and his work he contributed greatly to the success of the hospital. All at St. Hugh's would hope that in his Heaven there is a garden with woodlands and fruit trees, well-stocked beehives, a capacious tool-shed, and some fellow enthusiasts not as expert as himself.

H. C.

Appointments

LYONS, JOSEPH, M.B. Leeds, D.P.H.: M.O.H. and divisional M.D., West Riding, Yorks.

Colonial Service:

CACHIA, C., M.D., B.SC.: M.O., Kenya.
DOUGLAS, E. S. M., L.R.C.P.E.: acting M.O., Jamaica.
EGWUATU, S. O., M.B. N.U.I.: M.O., Nigeria.
LAVOIPIERRE, J. A. R., M.D. Paris, D.T.M., D.P.H.: deputy director of medical services, Mauritius.
LAYCOCK, H. T., M.A., M.B. Camb., F.R.C.S.: M.O. (surgical), British Somaliland.
O'MAHONEY, J. P., M.B. N.U.I.: chief M.O., Barbados.
PAGE, H. G., O.B.E., M.B. Edin., F.R.C.S., M.R.C.O.G.: surgeon specialist, Grenada, Windward Islands.
PEAT, A. A., M.B. Aberd.: director of medical services, Trinidad.
STEVENS, C. E. E., M.B. Belf., F.R.C.S.E.: superintendent, Cunningham Hospital, St. Christopher-Nevis.
STOBBS, J. E., M.B. Durh.: M.O., Nigeria.
STRISIVER, E. V., M.D. Berlin: M.O., special grade, Sierra Leone.
TOMLINSON, C. H., M.B. Edin.: radiologist, medical department, Jamaica.

Digitized by Google

Notes and News

TRAINING GRANTS FOR ASSISTANTS

THE Minister of Health has now notified executive councils of the terms under which practitioners may engage assistants for training under a system of Government grants; and he has suggested that principals should be invited to submit applications to take part in the scheme. The conditions are those outlined in last week's annotation (p. 656); and the announcement makes it clear that the practitioner whose application is approved will himself be responsible for appointing the assistant and for satisfying the executive council that the candidate appointed has not previously been in practice in the British Isles.

GLASGOW AND ITS ROYAL FACULTY

AT a meeting of the Scottish Society of the History of Medicine held in Glasgow on Oct. 20 with Dr. Douglas Guthrie in the chair, Prof. J. D. Mackie said that the University of Glasgow, founded in 1451, was at first modelled on French lines, but after the Reformation was reorganised by Andrew Melville. Mr. A. C. Goodall, librarian of the Royal Faculty of Physicians and Surgeons, said that the faculty was unique among medical corporations in this country in uniting surgeons with physicians. Founded in 1599 by Maister Peter Lowe it received its charter from James VI the same year. Among its many duties were the examination and licensing of all surgeons in the West of Scotland, supervision of their conduct, and ensuring the high quality of drugs. A service of free medical aid to the poor of the city was another noteworthy feature of the activities of the faculty, which next year will celebrate its 350th anniversary.

ICY CHRISTMAS

A BAD harvest nowadays is a disaster for the whole world; and the news that this year the granaries would be filled has been the one cheerful flourish in an otherwise bleak and only too convincing narrative of man's follies and misfortunes. In Labrador, where food is scarce at any time, the harvest is more elusive than elsewhere, being apt to swim off. For two summers fish have been scarce, and on land there have been few fur-bearing animals. This means a hard winter for the fisherman, hunters, and trappers, and their children. They will be hungry again, and cold. Many of their dogs, on which they depend for transport, have died, and more will die this year. The wooden hospitals and nursing stations, which have withstood forty years of arctic storms, need rebuilding; they are fuller than ever and badly need new X-ray equipment to help in the fight against tuberculosis, now on the increase.

The Grenfell Association, founded by Wilfred Grenfell to undertake medical work among British settlers in Labrador and Northern Newfoundland, has many friends on both sides of the Atlantic who like to help in its heavy and necessary task. One way to do it is to send out Grenfell Christmas cards, which are again available this year. The cards carry simple greetings only, and include several in colour: they range in price from 1*s.* 2*d.* to 6*d.* each, and there are also packets of six postcards at 2*s.* a packet, packets of six Christmas labels at 9*d.*, and some pleasant purse calendars at 3*d.* each; postage is extra. They may be bought from the Secretary, Grenfell Association, 56, Victoria Street, London, S.W.1.

PREVENTION OF DEAFNESS

IN the autumn of 1946, in the town of Lund, Dr. Nils Lundgren [1] examined 1426 children in the public elementary schools and found that 15–16% were more or less deaf on one or both sides. *Nordisk Medicin* [2] points out that in the national schools in Stockholm it has long been customary to test the hearing of each child once a year. In principle, the teacher who finds that a child cannot hear whispering at a distance of less than 3 metres on one side or other must report this to a school doctor. In Stockholm provision is made for the examination of deaf children once a week, and when enlarged adenoids are found they are removed. A somewhat similar system is in operation in Göteborg, Malmö, Lund, and Norrköping, but elsewhere in Sweden early cases of deafness are largely neglected, and often the patient does not see a specialist till his disability has become permanent. In the near future it is hoped that all the teeth of every Swedish child will be examined once or twice every year by a dentist; and it may be asked why there is no equivalent measure for the early detection and treatment of deafness. A child's lost teeth can to a certain extent be replaced by dentures, but there is no such effective substitute for good ears. Dr. Lundgren writes: "It is just as necessary for the otolaryngologist to examine the nasopharynx, tympana, and hearing of children once or twice a year in order to preserve their hearing as it is for the dentist to examine teeth at regular intervals."

1. *Nord. Med.* May 21, 1948, p. 1015.
2. *Ibid*, p. 1060.

Rh

Dr. Alexander Wiener, of New York, has circulated to various libraries bound copies of some of his contributions to the work on the rhesus factor. As he was, with Landsteiner, one of the original discoverers of this factor, the original papers are here reproduced; the latest reprint is from a journal dated April, 1948. Those who are studying the subject will be glad to have so much actual source material so conveniently presented. Some idea of the size of the literature that has grown up about Rh factors in a short time may be gathered from the bibliography of contributions from Dr. Wiener and co-workers, which total 179 papers published, with another 6 in the press. From the papers many more key references can be gathered.

FOOD RATIONS IN GERMANY AND AUSTRIA

ACCORDING to figures issued by Economic Coöperation Administration, the normal consumer ration in the Bizone of Germany now yields about 1850 calories per day, while the new ration for miners affords 4000 calories daily. The monthly meat ration is 300 g., compared with 100 g. last March. The over-all non-farm ration averages 2150 calories —a 15% improvement on the average a year ago. It is pointed out that before the late war Germany imported more than a third of her food. Moreover, it is expected that at the end of this year the combined population of the two zones will be 44 million, whereas before the war it was 34·2 million.

In Austria the normal ration was raised last month from 1800 to 2100 calories a day. Additional food allocated to workers in heavy industries has brought the average for the urban population up to 2300 calories; and in 1948–49 the average is expected to reach 2500–2600. In both countries the crops are very considerably better than last year.

THE HAVEN PRODUCTS SCHEME

THE success of a sheltered workshop turns on the good spirit of the workers; and this derives from their sense of personal achievement. Since to depend on charity always saps morale, the best sheltered workshops are those which are economically sound and pay a wage which owes nothing to outside benefactions. A particularly successful example is Haven Products,[1] opened on the Scottish Industrial Estate at Hillington, Clydeside, in 1946. The scheme was begun by doctors, social workers, and industrialists, all of whom accepted the principle of community responsibility for Service and industrial casualties. Most of the £6000 needed to start the enterprise was subscribed by industrialists on the estate. Later the project was incorporated as a private company in which profits, instead of being distributed to shareholders, go back into the workshop. The main work offered is the making of electrically heated pads and blankets; and Messrs. Thermega, who for many years, at Leatherhead, have been employing ex-Servicemen with neuroses in the manufacture of this equipment, offered a subcontract on favourable terms.

At Hillington the machines provided had to be specially modified for the use of physically disabled men, benches had to be designed to allow the chair-bound worker to get into a comfortable position, doors had to be wide enough to let invalid chairs pass easily, rest-rooms were needed, and water-closets had to be fitted with supporting rails. The place is cheerfully decorated and meals are available in a cafeteria on the ground floor.

The workshop opened in March, 1946, with two foremen, one storekeeper, and a manager. A week later 14 severely disabled men were in training, and there are now 45 at work,

1. Haven Products. By A. E. TURNER, T. A. STIRRAT, and Prof. T. FERGUSON, M.D. Brochure published by the Nuffield Provincial Hospitals Trust, 12 and 13 Mecklenburgh Square, London, W.C.1.

Digitized by Google

some with multiple disabilities. They work an 8-hour day on 5 days a week and earn a basic wage of 2s. 1½d. an hour plus bonuses. At present their homes are widely scattered, and they come to work by ambulance, motor chair, or public transport; but the Scottish branch of the British Red Cross is contributing funds to provide 20 houses for ex-Servicemen, through the Scottish Veterans' Garden City Association. The labour force was built up gradually as production developed.

Most of the men are severely disabled as a result of gunshot wounds of the head or spine, or such conditions as organic disease of the nervous system, heart disease, nephritis, rheumatoid arthritis, congenital muscular wasting, and amputations The average age is thirty-two, and 25 are married. In many cases an opportunity to earn a living has meant a complete change in outlook for the disabled man, from angry despair to keenness and self-confidence; and the workshop has about it an atmosphere which expresses the enthusiasm and sense of corporate life found among those employed there. As one of them wrote: "I know you'll appreciate how I feel at being able to keep the home fires burning off my own bat."

University of Oxford

On Oct. 14 the following degrees were conferred:

M.Ch.—E. G. Tuckwell.*
B.M.—E. J. E. Jones, R. G. Chambers, Zaida M. Megrah, Jean C. Toynbee, H. A. Evans,* A. R. Wilson,* J. W. Platt,* A. C. Cox.*

* In absentia.

University of Cambridge

On Oct. 16 the following degrees were conferred:

M.D.—O. C. Lloyd.
M.B., B.Chir.—Hugh Middleton,* John Wedgwood,* N. R. Greville,* Adrian Hill,* I. C. Peebles.*

* By proxy.

University of London

Mr. H. R. Ing, D.PHIL., will give a lecture at the London School of Hygiene, Keppel Street, W.C.1, on Friday, Dec. 3, at 5.15 P.M. He is to speak on the Pharmacology of Homologous Series.

University of Liverpool

Dr. Alexander Macdonald has been appointed to a readership in the department of bacteriology at the school of hygiene.

On Wednesday, Nov. 3, at 5 P.M., in the arts theatre of the University, Dr. Edward D. Churchill, John Homans professor of surgery at Harvard University, will deliver the William Mitchell Banks lecture. His subject is to be Wounds of the Chest—a Study of the Evolution of Method in Surgery.

University of Leeds

Dr. S. J. Hartfall has been appointed to the chair of clinical medicine in succession to Dr. Le Fleming Burrow who has retired.

Dr. Hartfall graduated M.B. at the University of Leeds in 1926, and after holding resident appointments at the Leeds General Infirmary he became medical assistant at Guy's Hospital. In 1931 he took his B.SC. and his M.D. with distinction, and the following year he was awarded a Leverhulme research scholarship for work on anæmia and gastric secretion. In 1937 he took up the chair of therapeutics and applied pharmacology at Leeds where he already held appointments on the staffs of the General Infirmary and Public Dispensary. He holds the Territorial rank of lieut.-colonel in the R.A.M.C. His published work includes papers on the function of the stomach and reports on the use of gold in rheumatic diseases as practised in the Leeds Public Dispensary. In 1940 he was elected F.R.C.P.

Dr. Louise Eickhoff has been appointed senior lecturer in child psychiatry.

Institute of Laryngology and Otology

On Friday, Nov. 19, at 4.30 P.M., Mr. Walter Howarth will deliver the annual address at the institute, 330, Gray's Inn Road, London, W.C.1. The title of his lecture is to be The End of an Era—a Retrospect and a Prospect.

Medical Women's Federation

The federation has moved from its war-time quarters in Kent, and its address is now Tavistock House North, Tavistock Square, London, W.C.1 (Tel.: Euston 7765).

Royal College of Physicians of London

Dr. Robert Coope is to give the Mitchell lecture on Thursday, Nov. 18, on Tuberculous Enlargement of Intrathoracic Lymph Nodes and its Aftermath. Dr. J. A. Charles will deliver the Bradshaw lecture on Tuesday, Nov. 23. He is to speak on Victorian Medical Administrators and their Significance for Today. Both lectures will take place at 5 P.M. at the college, Pall Mall East, S.W.1.

Royal College of Surgeons of England

A meeting of fellows and members will be held at the college, Lincoln's Inn Fields, London, W.C.2, on Wednesday, Nov. 10, at 5.30 P.M. On application to the secretary, fellows and members and other diplomates of the college can obtain copies of the report from the council which will be laid before the meeting. Motions to be brought forward must be signed by the mover, or by the mover and other fellows and members, and must be received by the secretary not later than Nov. 1. A copy of the agenda will later be issued to any fellow or member who may apply for one.

On Thursday, Nov. 11, Mr. L. E. C. Norbury will deliver the Bradshaw lecture on Proctology Throughout the Ages. On Wednesday, Nov. 17, Mr. Geoffrey Keynes will give the Thomas Vicary lecture on the Portraiture of William Harvey. On Thursday, Dec. 9, Sir Reginald Watson-Jones will give the Robert Jones lecture on the Reactions of Bone to Metal. All the lectures will be held at the college, Lincoln's Inn Fields, London, W.C.2, at 5 P.M.

Faculty of Anæsthetists.—At a meeting of the board of the faculty held on Oct. 6 Mr. A. D. Marston, the dean, introduced some 19 newly elected fellows who were admitted to the fellowship by Lord Webb-Johnson, the president of the college. It was decided that whereas up to the present only holders of the diploma in anæsthetics of the two Royal Colleges should be eligible for membership of the faculty, in future, holders of the diploma of other recognised bodies should be eligible. The first Joseph Clover memorial lecture, which has been founded by the faculty, will be given by Mr. Marston on March 16, 1949.

The following have been elected to the fellowship:

H. K. Ashworth, Wesley Bourne, S. F. Durrans, H. E. Karslake Eccles, A. H. Galley, Noel Gillespie, Victor Goldman, John Halton, A. E. W. Idris, R. W. Ironside, F. Barnett Mallinson, Mrs. H. Scott Mason, Mrs. K. L. Oldham, Mrs. E. M. Taylor, Ralph M. Waters, Keith Woodruff.

University College, London

Mr. B. C. J. G. Knight, D.SC., will give three public lectures, on Biosynthesis in Micro-organisms, on Thursdays, Nov. 11, 18, and 25. Prof. C. de Duve, who holds the chair of physiological chemistry in the University of Louvain, will lecture on Dec. 6, 9, and 13 on the Control of Carbohydrate Metabolism. All the lectures will be given at 4.45 P.M. in the physiology theatre of the college, Gower Street, W.C.1.

British Association of Physical Medicine

A course in preparation for part I of the diploma in physical medicine will be held at Guy's Hospital beginning on Jan. 10, 1949, if there are enough candidates. Further information may be had from the dean of the medical school, Guy's Hospital, London, S.E.1.

Farouk I University, Alexandria

Mr. G. H. C. Ovens, F.R.C.S., has been appointed professor of clinical surgery in the university. Mr. Ovens has held the posts of clinical assistant and surgical tutor at St. Mary's Hospital, London, and of surgeon in the E.M.S.

Federation of Committees for the Moral Welfare of Children

Today, Friday, Oct. 29, at 2.30 P.M., at the Caxton Hall, S.W.1, the federation is holding a conference on Marriage in Our Time. The speaker is to be Dr. Lilias Jeffries.

Wessex Rahere Club

The first annual dinner of this club was held at the Roya Hotel, Bristol, on Oct. 17. Dr. E. R. Cullinan attended from Barts as guest of honour and some 36 members were present under the chairmanship of Dr. G. D. Kersley. Membership is open to all Barts men resident in Somerset, Wiltshire, and Gloucestershire, and the hon. secretary is Mr. A. Daunt Bateman, 3, The Circus, Bath.

Digitized by Google

Intermediate Medical Certificates for Inpatients

It has been arranged that, to relieve the pressure on hospital medical staffs, these certificates may be signed by lay officers.

Blackcurrant Syrup

The Ministry of Food has made arrangements, similar to those for last year, to provide blackcurrant syrup and purée for sale through retail chemists for children up to the age of 18, invalids, and persons in need of additional vitamin C.

Royal Statistical Society

At a meeting of the research section to be held on Tuesday, Nov. 2, at 5.15 P.M., at the E.L.M.A. Lighting Service Bureau, 2, Savoy Hill, London, W.C.2, Prof. J. B. S. Haldane, F.R.S., will open a discussion on Statistical Problems Arising in Genetics.

W.H.O. Office in South-east Asia

At a conference in New Delhi early this month, representatives of India, Ceylon, Thailand, Burma, and Afghanistan—the five countries designated to form the South-east Asia regional committee of the World Health Organisation—recommended New Delhi as the site of the regional office.

Contamination of Food by Metals

The Food Standards Committee, appointed by the Minister of Food in January, has set up a subcommittee to inquire into the metallic contamination of foods. The members include: Prof. G. R. Cameron, F.R.S., Prof. S. J. Cowell, Dr. J. M. Johnston, Dr. W. P. Kennedy, and Dr. G. Roche Lynch.

Priority for Children's Teeth

In a statement issued on Oct. 18 the British Dental Association urges the Government to provide dental treatment for children even at the expense of the rest of the population. At present the heavy demands on the general dental service—including the repair and renewal of elderly and middle-aged dentitions—make it impossible to maintain recruitment to what should be the priority service. The association further points out that school dental officers are being offered salaries below the level recommended by the Spens Committee, and adds the warning: "Unless the Ministry of Health and the Ministry of Education take a responsible and constructive interest without delay, there is the gravest danger of the existing skeleton priority dental service for our children crumbling away into dust."

The Dental Service Association further add that the shortage can only be met by using all the dental resources of the country, and suggest that "if the Denture Repair Services were brought into the scheme, much of the work which is now unnecessarily engaging the energy of dentists could be taken off their hands."

Births, Marriages, and Deaths

BIRTHS

BARRAS.—On Oct 1, in Malta, the wife of Dr. B. W. Barras—a son.
BULSTRODE.—On Oct. 19, at Hartfield, Sussex, the wife of Dr. J. C. Bulstrode—a daughter.
ELEK.—On Oct. 1, the wife of Dr. Stephen Elek—a daughter.
GARVIE.—On Oct. 13, at Woking, the wife of Dr. J. M. Garvie—a son.
LAMBLEY.—On Oct. 15, at Northampton, the wife of Mr. D. G. Lambley, F.R.C.S.—a son.
LEWIN.—On Oct. 15, at Oxford, the wife of Mr. Walpole Lewin, F.R.C.S.—a daughter.
PARRY.—On Oct. 21, at Cardiff, the wife of Mr. J. N. M. Parry, F.R.C.S.—a daughter.
SEWARD.—On Oct. 21, in London, the wife of Dr. E. C. Seward—a daughter.
SUGARS.—On Sept. 29, the wife of Dr. J. C. Sugars—a daughter.
WRIGHT.—On Oct. 18, in London, the wife of Dr. E. G. Wright—a son.

MARRIAGES

CHILDS—FORBES.—On Oct. 16, at Frimley, John Michael Childs, M.B., to Elizabeth Sheila Forbes.
KNOWLSON—WILSON.—On Oct. 5, at Oxwich, Gower, George Akenhead Knowlson, M.A., to Lydia Annie Wilson, M.D.

DEATHS

GOVAN.—On Oct. 17, at Cockermouth, Cumberland, George Govan, M.B. Edin., aged 84.
INNES.—On Oct. 16, Edward John Innes, M.B. Lond., Flight-lieutenant, R.A.F., aged 26.

Diary of the Week

OCT. 31 TO NOV. 6

Monday, 1st

ROYAL COLLEGE OF SURGEONS, Lincoln's Inn Fields, W.C.2
3.45 P.M. Prof. F. Wood Jones, F.R.S.: Muscles of the Body Wall.
5 P.M. Dr. Cuthbert Dukes: Surgical Pathology of Intestinal Tumours.

SOCIETY OF APOTHECARIES, Black Friars Lane, E.C.4
5 P.M. Dr. Eliot Slater: Constitutional Factors in Psychological Medicine.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.2
2.30 P.M. Miss D. J. Collier: Facial Paralysis from the Otological Standpoint.

Tuesday, 2nd

ROYAL COLLEGE OF PHYSICIANS, Pall Mall East, S.W.1
5 P.M. Dr. Geoffrey Marshall: Tuberculosis of the Bronchi.

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. D. V. Davies: Middle Cranial Fossæ.
5 P.M. Dr. Dukes: Surgical Pathology of Intestinal Tumours.

SOCIETY OF APOTHECARIES
5 P.M. Dr. Peter Bishop: Use of Sex Hormones in Therapeutics.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, W.C.2
5 P.M. Dr. I. Muende: Histopathology of the Skin.

CHADWICK LECTURE
2.30 P.M. (Westminster Hospital medical school, Horseferry Road, S.W.1.) Dr. W. E. B. Lloyd: Prevention of Tuberculosis with Special Reference to Environment.

EDINBURGH POST-GRADUATE BOARD FOR MEDICINE
5 P.M. (Royal Infirmary.) Prof. J. W. McNee: Cirrhosis of the Liver.

Wednesday, 3rd

ROYAL COLLEGE OF SURGEONS
5 P.M. Prof. Ronald Hare: Staphylococci.

LONDON COUNTY MEDICAL SOCIETY
3 P.M. (Lambeth Hospital, Brook Drive, S.E.11.) Clinical meeting.

UNIVERSITY OF LIVERPOOL
5 P.M. (Arts Theatre.) Prof. Edward Churchill (Harvard): Wounds of the Chest—a Study of the Evolution of Method in Surgery.

Thursday, 4th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Sir John Parkinson: Aortic Stenosis.

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Prof. H. A. Harris: Nerve-supply of the Limbs.
5 P.M. Professor Hare: Staphylococci.

UNIVERSITY OF LONDON
5 P.M. (1, Wimpole Street, W.1.) Mr. G. Ewart Martin: Broncho-œsophagology in Great Britain. (Semon lecture.)

INSTITUTE OF DERMATOLOGY
5 P.M. Dr. G. B. Mitchell-Heggs: Complications in Eczema.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
2.30 P.M. Mr. J. Angell James: Diseases of the Antrum of Dental Origin.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY
3 P.M. (London Jewish Hospital, Stepney Green, E.1.) Mr. H. A. Levy: Æsthetics of Vision. (Presidential address.)

HONYMAN GILLESPIE LECTURE
5 P.M. (Edinburgh Royal Infirmary.) Mr. Robert Maller: Carcinoma of Rectum.

Friday, 5th

ROYAL COLLEGE OF PHYSICIANS
5 P.M. Dr. W. G. Oakley: Complications of Diabetes and their Treatment.

ROYAL COLLEGE OF SURGEONS
3.45 P.M. Professor Harris: Clinical Anatomy of the Abdomen.
5 P.M. Dr. R. J. Ludford: Cytopathology of Cancer.

SOCIETY OF APOTHECARIES
5 P.M. Prof. E. D. Dodds, F.R.S.: Endocrinology and its Relation to Diagnosis and Treatment.

LONDON CHEST HOSPITAL, Victoria Park, E.2
5 P.M. Mr. V. C. Thompson: Surgery of the Œsophagus.

On Oct. 5, at the Rikshospital in Oslo, Prof. F. G. Young, of University College, London, delivered the third Jacobaeus lecture, founded in memory of Prof. H. C. Jacobaeus, of Sweden, who died in 1937. He spoke on the Relation of the Pituitary Gland to Diabetes Mellitus.

Mr. A. G. Timbrell Fisher has been elected to the fellowship of the American College of Surgeons.

CORRIGENDUM: *Œstrogens in Diabetes.*—Ref. 3 on p. 659 should read Biskind, M. S., Schreier, H. *Exp. Med. Surg.* 1945, 3, 299.

Digitized by Google

Digitized by Google

Digitized by Google

Digitized by Google

Digitized by Google

Dec26'67

Feb7'66

Nov25'68

47182

Lancet

Sept.-Oct., 1948 v.2

Lancet 47182
Sept.-Oct., 1948 v.2

Iowa State Medical Library
HISTORICAL BUILDING
DES MOINES, IOWA

We hope you obtain pleasure and profit from the use of the Iowa State Medical Library. You can increase its usefulness by returning your books promptly. We are pleased to be of service to you.

Borrower. Adults are entitled to draw books by filling out an application card.

Number of Volumes. Two new books, or two new consecutive Journals cannot be taken by one person. Students may borrow 3 volumes at a time, which are not renewable.

Time Kept. The period of loan is two weeks; older books may be once renewed. New books and Journals are not renewable.

Forfeiture of Privilege. Loss of books or journals without paying for same, defacing or mutilating materials, three requests for postage without results, three requests for return of material without results, or necessity of asking Attorney General's aid to have material returned, bars from future loans.

Transients and those at hotels may borrow books by depositing the cost of the book, or $5.00, which is returned when the book is returned.

Digitized by Google